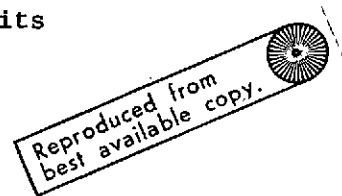*ϒ*

# FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM
## UNDER THE COMBINED EFFECT OF STRESS FACTORS
### (Ionizing Radiation, Accelerations and vibration)

Editor in chief

N. N. Livshits

Translation of "Funktsii tsentral'noy nervnoy
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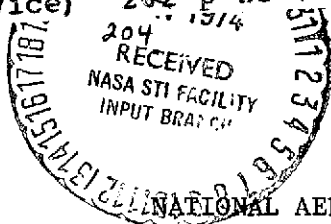pp 1- 174

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In fond memory of
Academician
Vasiliy Vasil'yevich
Parin

# NEW DATA ON THE COMBINED EFFECT OF SPACE FLIGHT FACTORS
## ON THE CENTRAL NERVOUS SYSTEM

N. N. Livshits

Numerous studies of the combined effects of|various stress agents, infec-    /5*
tions, mechanical traumas, burns, ionizing radiations, etc., have shown that
with a combined force the reactions of the organism differ significantly from
those we are used to observing with each of these agents individually and are
often unexpected [1, 35, 36, 37, 38, 39, 42, 43, 44].  Therefore, in order to
predict the effects of space flight factors it is necessary to know the laws of
their combined action.

Works dealing with this question are systematized and summarized in
reviews of literature [9, 22, 38, 39].

Of obvious interest to space biology is a study of the effect of dynamic space |
flight factors and ionizing radiations on the function of the central nervous
system.  The central nervous system (CNS) is not a critical organ for radiation
or for dynamic factors, but man's ability to work is determined by the functional
state of this system.  In addition, these studies are theoretically important
for understanding the laws and mechanisms of reactions to stress forces.

The group of authors contributing to this collection have been studying
for a number of years the effect of ionizing radiations in combination with
accelerations or vibrations on the function of various sections of the central
nervous system.   Results of these works have been cited in preceding |collec-
tions and review articles [10, 11, 24, 32, 43].  In our earlier works we estab-
lished several laws of the combined action of dynamic and radiation factors.  It
was found that reactions of the central nervous system to combined forces are of

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*Numbers in the margin indicate pagination of original foreign text.

the following basic types:

1.  Domination of the effect of the dynamic factor at all stages.

2.  Predominance of the dynamic effect in early stages after the combined force and the radiation effect at later stages or the same course of reaction as indicated above soon after the force, giving way in after-action to the combined effects of both factors; also possible are partial summation, mutual /6 weakening and reproduction of the direction of one of the factors and the dynamics of processes typical of the other.

3.  A reaction to the combined force which is intermediate between reactions to each of the agents applied individually.

4.  Predominance during the entire period of observations of the dynamic factor in some groups of animals and of the radiation effect in other groups.

5.  Mutual intensification of the effects of the dynamic and radiation factors during the entire period of observations.

These reactions are varied, but the first four are distinguished by high reproducibility.

For combined forces we used lateral accelerations with an intensity of 8-10 g lasting from 4 to 15 minutes, vertical vibration (70 cps, 0.4 mm, 15 min.) and radiation in doses from 50 to 600 r lasting from 2 minutes to 14 hours, as well as radiation in fractional doses. We studied unconditioned cerebrospinal reflexes, electromyographic responses of extensors of hind limbs to adequate stimulation of the vestibular analysor, conditioned reflexes to food, behavior of rats in a maze and the intensity of respiratory metabolism in brain tissues. We observed these types of reactions in studying all the above indices (with the noted parameters of effective factors) which indicated the general character of these laws.

We found no basic difference between the influence of accelerations and vibration on the radiation effect. This agrees with the results of studies of the effect of these agents combined with radiations on other functions of the body [39].

The differences between the combined action of vibration or accelerations and radiation in our tests were primarily the fact that the dynamic factor predominated in a more pronounced manner when accelerations were used.

Earlier it was shown that reactions of the vestibular analysor to radiation significantly changed under the influence of accelerations applied 3 days before radiation [8]. We have not yet studied longer after-action of the dynamic factor. In the two works of Z. I. Apanasenko published here, guinea pigs were radiated in a back-chest direction 7 days after acceleration with an intensity of 10 g and exposure of 15 and 4 minutes.

With both kinds of force, the influence of the dynamic factor on the radiation effect was very pronounced. It also appeared in studying a factor which had already returned to its original level by the time of radiation (the latent period of the vestibulotonic reflex in both works).

The influence of preliminary centrifuging on the effect of radiation in /7 both variants of the test was so great that we can assume a seven-day interval between these factors is not maximum.

Reactions to combined forces in the majority of cases were the same basic types observed with radiations conducted several minutes after the application of the dynamic factor.

The latent period of the vestibulotonic reflex and the integral bioelectric activity of tested muscles during adequate stimulation of the vestibular apparatus in animals exposed to 4-minute centrifuging changed according to the second type. In less distinct form, this type of reaction was detected in the changes in spontaneous bioelectric activity of muscles and the length of the after-action of adequate stimulation of the vestibular analysor in the same animals.

A variation of this type is changes in the spontaneous bioelectric activity of extensor muscles after the combined force of 15-minute centrifuging and radiation.

The third type of reaction was observed in the same animals in studying the duration of the after-action of adequate stimulation of the vestibular analysor and the electric activity of muscles during this period in animals exposed to 4-minute centrifuging, etc.

The fourth type of reaction was very pronounced in changes in the latent period of the vestibulotonic reflex after the combined force of 15-minute centrifuging and radiation.

In all these cases the radiation effect under the influence of acceleration

was weakened either soon after the action, or in part of the animals, or to some degree throughout the entire period of observations. Sometimes the effect of radiation in the case of a combined force was indistinguishable. This effect of accelerations can be considered radioprotective.

However, as indicated in enumerating the types of reactions to a combined force, we also noted earlier the possibility of intensification of the radiation effect (fifth type). We observed this type of reaction previously in only two cases: in studying the effect of three vibrations with subsequent radiation in a dose of 50 r on conditioned reflexes of rats [25] and in studying the effect of centrifuging 3 days before radiation on radiation reactions of the vestibular analysor [8]. In none of the other works could it be found. This type of reaction was not seen, in particular, in studying the effect of these same factors on maze learning of rats [40, 41]. For this reason, in our previous publications we did not separate this reaction into an independent type, only mentioning it in describing specific tests [8, 25]. We felt it necessary to prove these data. There were also other bases for setting up additional studies. Up to now in the above publications, we have emphasized the general laws of reactions of various functions of the central nervous system to the combined force of dynamic and radiation factors. But there is undoubted interest in studying the characteristics of individual functions and finding out which functions are most damaged. We assumed that conditioned reflexes are more strongly impaired and maze learning more easily compensated during unfavorable forces. The basis for such an assumption was a long discussion between researchers using conditioned reflex and maze methods.

The first described the unfavorable effect of radiations in doses of 50-200 r on several indices of conditioned reflex activity. The second found no deterioration of test indices as the result of these and higher doses [15, 20, 23, 45]. I. P. Pavlov [33] in a discussion with K. S. Leshli indicated that a rat in a maze can make use of signals from various analysors, creating greater possibilities for compensation in case of surgical injury of the brain. We voiced the opinion that this indication of I. P. Pavlov could also be extended to radiation damage to the central nervous system [23]. Earlier published works of Ye. M. Skobeyev [40, 41]* have indicated that this theory can also be

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*See also the article of Ye. M. Skobeyev in this collection.

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extended to the effects of dynamic factors and combined forces.

Study of the possible summation of radiation and vibration effects and the characteristics of vibration, radiation and a combination of these agents on conditioned reflexes and maze learning were dealt with in two articles by N. N. Livshits, Ye. S. Meyzerov et al. in this collection.

Two versions of the test were conducted.

1. The effect of three x-ray radiations in single doses of 50 r and general vertical vibration (70 cps, 0.4 mm, 15 min.) was studied as well as the combination of these factors on the conditioned reflexes of rats under the same methodological conditions used previously by Ye. M. Skobeyev to study the effect of these actions on maze learning.

2. In these same rats both conditioned reflexes and maze learning were developed and then the effect of a single x-ray radiation of 100 r, vibration, and the combined action of these agents was studied in both kinds of higher nervous activity. The two versions of the test gave basically the same results.

The first work established that three vibrations, radiation and a combination of these factors, which in the tests of Ye. M. Skobeyev caused no reliable deterioration of maze learning, led to a statistically significant increase in the latent periods of conditioned reflexes. /9

In the second study, forces causing statistically reliable deterioration of several indices of conditioned reflexes had no such effect on maze learning in these same animals. Results of these tests show that different kinds of higher nervous activity differ in reliability and, therefore, are disturbed to varying degrees under the influence of dynamic and radiation factors.

Using the conditioned reflexes method in the second version of the test it was also possible to detect a stable increase in the radiation effect under the influence of preliminary vibration which indicates the reality of the fifth type of reaction to a combined force. In addition, the rarity of this form of reaction is also verified. Unlike the preceding work [25], no summation of vibration and radiation effects was found in the first version. These data show that the effect of radiation on functions of the CNS under the influence of vibration is increased only under certain conditions which also, evidently, explains the difficulty of reproducing this phenomenon.

The mechanism of the action of dynamic factors on radiation effects is of great interest. N. V. Sokolova [42] presents experimental proofs of the dependence of radiosusceptibility of tissues and organs on the level of their functional activity during radiation. In the effects we observed this mechanism evidently has no decisive value.

In the system of the vestibular analysor, as shown by the tests of Z. I. Apanasenko (published here), which are in complete agreement with the results of her previous works [5, 8], after accelerations functional activity was sharply increased for a long time. This did not, however, prevent a radioprotective effect. A radioprotective effect of accelerations was also observed on conditioned reflexes, which under the influence of this factor were sharply depressed for a long time [26].

It is interesting to note the opinion of authors who feel that an important role in the radioprotective effect of accelerations is played by hypoxia of the hypothalamus, increasing the activity of the hypophysis-adrenal cortex system [14, 39]. Data has already been accumulated on the participation of nonspecific adaptation mechanisms in the effects of the combined force of radiation and nonradiation factors [38, 39]. P. D. Gorizontov and I. A. Rudakov [13], by means of daily electric skin pain stimuli, caused an adaptation syndrome in rats. Death from gamma-radiation in a dose of 700 r was lower at the stage of resistance and higher at the stage of exhaustion than in the control.

Schildt and Thoren [47] connect the development of phases of the adapta-  /10 tion syndrome with dependence of the effects of combined forces on the time of actuation of stress agents. If at first a lesser trauma is inflicted and it is intense enough to cause a systemic reaction but is not so great as to destroy protective mechanisms, the resistance of the organism is increased and a succeeding more severe trauma is better tolerated. If a more severe trauma is inflicted first, the resistance of the organism is reduced. (It is very difficult to evaluate the intensity of different kinds of forces. The authors of this article suggest expressing the intensity of forces in lethal doses, but from our point of view this is possible only in some cases).

There are experimental data which point out the dependence of results of a combined force on the time of infliction of combined traumas.

Koslowskiy and Messerschmidt [46] showed that the infliction of a standard

surgical wound before radiation (510 r) reduced mice mortality. If the wound was inflicted an hour after radiation, death increased only slightly but infliction of such a trauma 4 days after radiation sharply increased mortality.

P. P. Saksonov et al. [39], on the basis of analysis of a great deal of experimental data in which various indices were used, came to the conclusion that if the dynamic factor (vibration or acceleration) is applied before radiation, the radioprotective action prevails; if the animals are exposed to radiation before the dynamic factor, more often the radiation effect is aggravated. The participation of nonspecific adaptation mechanisms is also indicated because optimum intervals of time between acceleration and radiation are found, favoring both a protective and a reinforcing effect [12, 27, 48].

The ability of accelerations to alter nonspecific resistance of the body was shown in the work of V. V. Antipov et al. [2]. These authors found that the tolerance of mice to physical load undergoes phase changes after accelerations with an intensity of 8 g in a chest-back direction for 20 minutes. Phase changes in resistance to physical load correlated with the dynamics of changes in the activity of ceruloplasmin in the blood.

It can be considered proven that factors nonspecifically increasing resistance also raise radioresistance and that accelerations with parameters close to those applied in our studies affect nonspecific resistance. It could, therefore, be expected that the mechanism of the increase of nonspecific resistance would play an important role in the radioprotective effect of accelerations described by Z. I. Apanasenko. However, in comparing the results of our /11 experiments with data of other authors we have still found no proofs of this theory. The dynamics of changes in radioresistance in our tests and in nonspecific resistance do not correlate according to literature data.

In studying the combined force of accelerations and radiations on conditioned reflexes, we observed some radioprotective effect in tests in which radiation occurred 5 minutes after the dynamic factor [26]. V. V. Antipov et al., found no changes in the tolerance of mice for physical loads 15 minutes after acceleration. An increase in total resistance was registered later in these tests. According to the data of P. D. Gorizontov and I. A. Rudakov [13], in rats on which pain stimuli were inflicted, radioresistance did not change in the mobilization phase. In the schemes of Schildt and Thoren [47] the depen-

dence of radioresistance only on phases of resistance and exhaustion is also
considered.

In the tests described by V. V. Antipov et al., [2] general resistance of
mice was sharply reduced on the 3-4th day after the force and increased on the
7th day.  Z. I. Apanasenko observed a radioprotective effect of accelerations
on the function of the vestibular analysor at both these times [8] (see the
article in this collection).  But it must be taken into account that para-
meters of the dynamic factor in the compared studies, although not sharply
differentiated, were not strictly identical.  Species characteristics of
the animals could also have played a role (Table 1).

Table 1

PARAMETERS OF ACCELERATIONS AND KINDS OF ANIMALS USED IN THE EXPERIMENT

| Author | Direction of accelerations | Intensity, g | Length of forces, minutes | Kind of animal |
|---|---|---|---|---|
| V. V. Antipov et al. [2] | Chest-back | 8 | 20 | Mouse |
| Z. I. Apanasenko [8] | Back-chest | 8 | 15 | Guinea pig |
| Z. I. Apanasenko (see this collection) | Back-chest | 8 | 15 | Guinea pig |
| N. N. Livshits et al. [26] | Back-chest | 10 | 8 | Rat |

This material gives no basis for justifying the role of nonspecific
changes in resistance in the combined effect of accelerations and radiation on
the functional state of the vestibular analysor, but neither does it give
cause to reject this suggestion absolutely.  This question requires further
research.

It is also necessary to study the specific action of dynamic factors on       /12
radiation effects.  The specific effect of vibration on radiation reactions is
revealed in the work of L. D. Luk'yanova and L. M. Murashko in this collection.

Earlier L. D. Luk'yanova showed that general vertical vibration (70 cps,
0.4 mm, 15 min.) causes two-phase changes in oxidizing metabolism of brain tis-
sues of rats: an initial increase of oxidizing processes, giving way 10-15 min.
after termination of exposure and sometimes even before the end  to inhibition
of these processes.

Exposing rats to radiation 15 minutes after vibration, L. D. Luk'yanova found a radioprotective effect of the dynamic factor not only in the indices of respiratory metabolism of nerve tissue but also in leukopenic reaction and survival of the animals [28]. The author voiced the opinion that stimulation caused by increased peripheral pulse during vibration is replaced in after-action by a state of maximum inhibition and resultant depression of oxidizing processes. The latter, as is known, has a radioprotective effect. But in that case, it is to be expected that radiation conducted against a background of postvibration stimulation and increased oxidizing metabolism would not be weakened, but can even be intensified. It was experimentally proved in the work published in this collection. In rats radiated 3 minutes after vibration life was reliably shorter than in the group exposed to radiation 15 minutes after vibration. Moderation of radiation leukopenia was observed only in animals radiated 15 minutes after vibration. This also corresponds to weakened radiation changes in oxidizing metabolism of nerve tissue.

Correlation between radioresistance and phase changes in oxidizing metabolism, inherent in vibration, verifies the specificity of this effect.

To understand the causes for modification of radiation effects in the combination of radiations and dynamic factors, further study of the mechanisms of the effect of dynamic factors on the body is necessary. New data on this question are contained in the second article by L. D. Luk'yanova and L. M. Murashko. The authors studied the effect of vibration on oxidizing metabolism of brain tissues of rats in tests in vivo and in vitro. The same phase changes in oxidizing metabolism were noted in the effect of vibrations on slices of cerebral cortex in vitro as with vibration of the entire animal organism. But with vibration of slices of the brain, the effects of the dynamic factor were weaker. This indicates the presence of common mechanisms in reactions to vibration in vivo and in vitro and, what is especially important, illustrates the /13 direct effect of this factor on nerve tissue. In addition, the weakening of the vibration effect in vitro confirms the presence in the body of factors intensifying the effects of direct vibration. This agrees very closely with the results of previous works of this author [29, 30] which showed that increased peripheral pulse plays an important role in the effect of vibration on oxidizing metabolism and the functional state of the central nervous system.

All this must be taken into consideration in evaluating the mechanism of vibration.

Calculating the specific and nonspecific action of dynamic factors on radiation effects presents considerable difficulties and study of the mechanism of the combined force requires even greater experimentation.

Until now we have considered the combined action of dynamic and radiation factors in relation to weakening and intensifying their effects. This side of the question has also been given greatest attention in the literature. But it would be a mistake to interpret the results of the combined effect| of ionizing radiations and factors of a nonradiation nature only as quantitative changes in the effectiveness of the forces. Qualitative changes in the effects are very important. They are of the above-described second type of reaction when, because of the domination of one of the effective factors, there is a complex interaction between both agents which becomes apparent in various forms. Cases have been described when after the combined force the direction of changes in the test index reproduced an effect typical of one of the joint factors and the dynamics of changes corresponded to the other factor [4, 19]. The effects of combined factors were mutually intensified when they were weak and weakened when they were strong. We turned our attention to the similarity between these changes and parabiosis [22]. A new verification of this comparatively rare phenomenon was obtained in the first work of Z. I. Apanasenko in this collection. Changes in spontaneous bioelectric activity of extensor muscles of the hind limb of guinea pigs under the influence of acceleration are wave shaped. After the combined force this index also changed in similar fashion but was in antiphase to changes registered in centrifuged animals. This makes it extremely probable that changes in intracentral relations, possibly of a parabiotic nature, take part in this phenomenon. There are many indications that the effect of a combined force depends on the parameters of the combined factors [14, 16, 34, 38, 39]. Therefore, it becomes necessary to study the dependence of radiation effects on the time factor. The importance of such studies is dictated by the following: 1) in space flight prolonged /14 radiations with various dose rates are possible; 2) the effects of the combined force of a dynamic factor and radiation depend on the dose rate of the latter [7] and 3) the role of the time factor in reactions of the central nervous sys-

tem to radiation have received inadequate investigation and in recent| years|
contradictions have been found in studies of this question.

In our previous works we came to the conclusion that prolongation and
fractionation of radiations do not moderate its effect on the function of the
central nervous system. In some cases prolonged radiations were slightly more
effective than brief actions [3, 6, 17, 21, 31]. However, M. A. Kuznetsova [18]
in tests on guinea pigs found that change in the functional characteristics of
the unconditioned reflex to a pain stimulus of the limb during fractionated ra-
diations is directly dependent on the rate of doses of radiation. In the
article by this author published in our collection it is verified that the
direct dependence of changes in this index is also maintained when brief and
prolonged| radiations, are compared. Parameters of radiations were identical to
those used by Z. I. Apanasenko [7]. She found no direct dependence of reactions
of the vestibular analysor on dose rate during radiation. It was necessary to
find the causes for contradictions in the results. To eliminate the effect of
individuality of the animals and the intereference of factors not under the
control of the experimentor, cerebrospinal defensive reflexes and the functional
state of the vestibular analysor were tested on the same days in the same ani-
mals (Z. I. Apanasenko, M. A. Kuznetsova, see this collection). The results
previously described by each of these authors individually were verified.
Changes in cerebrospinal reflexes were in direct relation to dose rate. Changes
in the functional state of the vestibular analysor were not weakened during
prolonged radiation, but were even intensified in several indices. A slight
increase in reactions to brief radiation,|in comparison with prolonged,|was ob-
served only at remote times after radiation.

In the previous work of Z. I. Apanasenko [7] comparison of such a remote
after-action of acute and prolonged radiations was impossible. In her pre-
viously-published tests dose rate of brief radiation was higher and after an
acute force the animals died during the first two weeks. Such differences in
relation to the time factor in two kinds of unconditioned reflex activity at
different levels of the central nervous system are still difficult to explain.
It can only be said that they, evidently, are connected with afferent and cen-
tral links of reflector arcs as the test reflexes have a common efferent| link.    /15
It is possible that here a role is being played by the greater complexity of

the central link of the vestibulotonic reflex. As is known, many centers of the brain and a large number of synapses take part in this reflex. But how this can affect the time factor in the action of radiations on these functions is unclear and this question requires further study. For the present we must take into account these characteristics of radiobiological reactions of the tested reflexes in predicting the action on them of radiation and the effects of the combined force of radiations and dynamic factors.

## REFERENCES

1.  Aleksandrov, N.N., S.V. Ryzhkov, L.S. Sukovatykh, I.A. Chalisov, G.B. Chesnokov, Ye.I. Kiseleva, R.N. Bubnova and I.G. Ramzen-Yevdokimov. Raneniya cherepa i golovnogo mozga (Injuries of the Skull and Brain). Leningrad, Medgiz, 1962.

2.  Antipov, V.V., B.I. Davydov, E.F. Panchenkova, P.P. Saksonov and G.A. Chernov. Kosmicheskiye issledovaniya, Vol. 2, No. 5, 1964, p. 797.

3.  Apanasenko, Z.I. Radiobiologiya, Vol. 1, No. 1, 1961, p. 45.

4.  Apanasenko, Z.I. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka," 1964, p. 92.

5.  Apanasenko, Z.I. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966.

6.  Apanasenko, A.I. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 197.

7.  Apanasenko, Z.I. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 218.

8.  Apanasenko, Z.I. In the book: "Nekotorye voprosy kosmicheskoy neyro-fiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 184.

9.  Benevolenskiy, V.N., V.S. Vasil'yev and M.G. Petrovnin. In the book: "Aviatsionnaya i kosmicheskaya meditsina" (Aviation and Space Medicine), Moscow, 1969, p. 57.

10. Collection: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System), Moscow, "Nauka", 1964.

11. Collection: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966.

12. Gaydamakin, N.A., V.G. Petrukhin, V.V. Antipov, P.P. Saksonov and V.S. Shashkov. Izv. AN SSSR, Biology series, Vol. 3, 1966, p. 346.

13. Gorizontov, P.D. and I.A. Rudakov. Patolog. fiziologii i eksperimental'- naya terapiya, Vol. 17, No. 2, 1964, p. 17.

14. Davydov, B.I., V.V. Antipov, N.I. Konnova and P.P. Saksonov. Kosmicheskiye issledovaniya, Vol. 3, No. 5, p. 789.

15. Kimel'dorf, D. and E. Khant. Ioniziruyushchiye izlucheniya: tsentral'naya nervnaya sistema, povedeniye (Ionizing Radiations: The Central Nervous System, Behavior). Moscow, Atomizdat., 1969.

16. Konnova, N.I. In the book: "Problemy kosmicheskoy meditsiny" (Problems of Space Medicine). Moscow, "Nauka", 1966, p. 218.

17. Kuznetsova, M.A. Radiobiologiya, Vol. 1, No. 1, 1961, p. 58.

18. Kuznetsova, M.A. In the book: "Nekotorye voprosy kosmicheskoy neyro- fiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 93.

19. Kuznetsova, M.A. In the book: "Nekotorye voprosy kosmicheskoy neyro- fiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 125.

20. Lebedinskiy, A.V. and Z.N. Nakhil'nitskaya. Vliyaniye ioniziruyushchikh izlucheniy na nervnuyu sistemu (The Effect of Ionizing Radiations on the Nervous System). Moscow, Atomizdat., 1960.

21. Livshits, N.N. Vliyaniye ioniziruyushchikh izlucheniy na funktsii tsen- /16 tral'noy nervnoy sistemy (The Effect of Ionizing Radiations on the Functions of the Central Nervous System). Moscow, Izd-vo AN SSSR, 1961.

22. Livshits, N.N. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 5.

23. Livshits, N.N. Radiobiologiya, Vol. 7, No. 5, 1967, p. 790.

24. Livshits, N.N., Z.I. Apanasenko, V.Ya. Klimovitskiy, A.P. Korolevskiy, M.A. Kuznetsova, L.D. Luk'yanova and Ye.S. Meyzerov. Uspekhi sovremennoy biologii. Vol. 67, No. 2, 1969, p. 256.

25. Livshits, N.N. and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 236.

26. Livshits, N.N., Ye.S. Meyzerov, R.M. Zakirova and V.A. Tikhaya. In the book: "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 169.

27. L'vova, G.S. Izv. AN SSSR, Biology series, Vol. 3, 1966, p. 355.

28. Luk'yanova, L.D. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 145.

29. Luk'yanova, L.D. and S.M. Ambrosova. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 95.

30. Luk'yanova, L.D., A.V. Kol'tsova, Ye.S. Meyzerov and Ye.P. Kazanskaya. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 105.

31. Meyzerov, Ye.S. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 180.

32. Nekotorye voprosy kosmicheskoy neyrofiziologii (Some Questions of Space Neurophysiology). Collection of articles. Moscow, "Nauka", 1967.

33. Pavlov, I.P. Polnoye sobraniye sochineniy (Complete Collected Works) Moscow-Leningrad. Izd-vo AN SSSR, Vol. 3, Book 2, 1951, p. 175.

34. Parfenov, G.P. Kosmicheskiye issledovaniya, Vol. 3, No. 4, 1965, p. 643.

35. Perelomy kostey i povrezhdeniya sustevov pri luchevoy bolezni (Bone Fractures and Joint Injuries in Radiation Sickness). Collection of articles. Moscow, "Meditsina", 1967.

36. Petrov, I.P. Fiziologicheskiy zhurnal SSSR. Vol. 10, 1960, p. 1224.

37. Petrov, I.P. Vestnik AN SSSR, Vol. 5, 1962, p. 87.

38. Rayevskaya, S.A. and Yu.G. Grigor'yev. In the collection: "Biologicheskoye deystviye protonov vysokikh energiy" (The Biological Effects of High Energy Protons). Moscow, Atomizdat, 1967, p. 71.

39. Saksonov, P.P., V.V. Antipov and B.I. Davydov. Ocherki kosmicheskoy radiobiologii (Outlines of Space Radiobiology). Moscow, "Nauka", 1968.

40. Skobeyev, Ye.M. Radiobiologiya, Vol. 10, No. 4, 1970, p. 619.

41. Skobeyev, Ye.M. Radiobiologiya, Vol. 10, No. 5, 1970, p. 715.

42. Sokolova, N.V. "Rol' funktsional'noy nagruzki v lokalizatsii luchevogo porazheniya" (The Role of Functional Load in Location of Radiation Injury). Tomsk, Izd-vo Tomsk. gos. un-ta, 1962.

43. Frank, G.M., N.N. Livshits, M.A. Arsen'yeva, Z.I. Apanasenko, L.A. Belyayeva, A.V. Golovkina, V.Ya. Klimovitskiy, M.A. Kuznetsova, L.D. Luk'- yanova and Ye.S. Meyzerov. Izv. AN SSSR, Biology series, Vol. 5, 1966, p. 625.

44. Khromov, B.M. Kombinirovannye luchevye porazheniya (Combined Radiation Injuries). Leningrad, Medgiz., 1959.

45. Turchtgott, E.J. Psychol. Bull. Vol. 60, 1963, p. 157.

46. Koslowski, L. and O. Messerschmidt. In: "Proc. of the International Medical Defense Symposium on Combined Injuries and Shock. Uppsala, June 3-6, Stockholm, 1968, p. 21.

47. Schildt, B. and L. Thoren. In: "Proc. of the International Medical Defense Symposium on Combined Injuries and Shock", Stockholm, 1968, ·p. 21.

48. Zellmer, R.W., G.J. Womack, R.C. McNeel and C.R. Allen. Aerospace Medicine, Vol. 34, No. 7, 1963, p. 626.

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# THE COMBINED EFFECT OF DYNAMIC FACTORS
## AND IONIZING RADIATIONS
## ON FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM


## STUDY OF THE REMOTE AFTER-ACTION OF ACCELERATIONS
## ON THE REACTION OF THE VESTIBULAR ANALYSOR
## TO| RADIATION

Z. I. Apanasenko


Long space flights and the establishment of orbital stations increases the
urgency of the question of different kinds of combined force of radiation and
dynamic factors of a nonradiation nature on the body.  A number of studies in
recent years have shown that the preliminary effect of acceleration increases
survival and length of life after radiation [10, 12, 8, 26, 22, 25, etc.].
True, the protective effect of the dynamic factor is usually small and some-
times completely absent; in some cases the outcome of radiation sickness is
also aggravated [9, 23, etc.].

A  certain degree of protective effect of preliminary centrifuging is also
noted in the majority of works dealing with study of changes in the chromosome
apparatus of plant and animal cells [1, 2, 3, 27, etc.].  However, there are
also studies which detected the opposite effect of the dynamic force [18].

Radiation changes in the system of hematogenic organs and peripheral blood
also depend (they usually decrease) on the preliminary effect of dynamic fac-
tors [12, 8, 7, 9].  The characteristics of the joint effect of accelerations
and radiation on the morphology and function of other systems (particularly
the nervous system) of the body have received very little study.  It has been
shown that vibration significantly alters the effect of radiation on oxidizing
processes in brain tissue [15], the duration of the latent period of the uncon-
ditioned passive-defensive reflex [11] and conditioned reflex activity in rats
[13].  The effect of radiation on higher nervous activity is also altered by

preliminary centrifuging [14].

There has been practically no investigation of the combined effect of accelerations and radiations on the vestibular analysor. Only a change in the /18 reactivity of the vestibular apparatus to Coriolis acceleration under the influence of penetrating radiation has been detected [17]. In our previous works [4, 5, 6] we showed that vibration and centrifuging significantly modify the effect of radiation on vestibular functions. Dynamic forces largely reduce radiation effects, mask them and sometimes completely determine the general result of a combined force. However, the relationship between effective factors is quite complex and diverse; it is far from always possible to predetermine the character of changes in a test index in cases of combined forces.

One of the main determinants here is, evidently, the time interval between respective factors. In the literature there are already direct indications that the effect of a combined force depends not only on the value and intensity of effective factors, but also on the interval between them [7, 16, 26]. Accordingly, this work was conducted to determine the existence and the character of a modifying effect of acceleration on subsequent radiation reactions when there is a considerable interval of time between these forces.

We studied electromyographic indices of the vestibulotonic reflex to adequate stimulation of the vestibular apparatus when the animal was subjected to measured swinging around the long axis of the head. After stable values were established for test parameters (4-8 days), the animals were exposed to 15-minute centrifuging (acceleration 8 g, back-chest direction). After 7 complete days they were exposed to general radiation (Co$^{60}$, 500 r, dose rate 168 r/min.). The animals were examined 1, 3 and 6 days after centrifuging and then 1, 2, 3, 5, 6, 10, 15 and 20 days after radiation. Three control groups of animals underwent parallel examination: a group exposed only to centrifuging, a group exposed only to radiation and a group kept under identical conditions but exposed to no forces (except the noise of the centrifuge and trips to the source of radiation and acceleration).

The study was conducted on male guinea pigs weighing 270-400 g. The functional state of the vestibular analysor was evaluated by electromyographic characteristics of the vestibulotonic reflex in muscles of hind limbs. The procedure, means of recording myoelectric characteristics, adequate stimulation

of the organ of balance and analysis of results are given in our previous works [5, 6].

The experiments revealed that with even a week interval between forces the influence of centrifuging on radiation effects is very clear. Fig. 1 shows the change in spontaneous electric activity of tested muscles after the combined (with an interval of 7 days) and isolated forces of acceleration and radiation. With centrifuging alone myoelectric activity in a state of relative quiet increases sharply. This rise is maintained during the entire first week after the force. During the next few days the electric activity of muscles fluctuates in a wave-like manner, but on the average continues to exceed the original level for a prolonged period. With radiation alone spontaneous bioelectric activity of tested muscles is reduced, beginning even on the first day after the force. Maximum reduction is reached by the 7-10th day after which the level of myoelectric activity does not change significantly up to death of the experimental animals. The effect of the combined force of centrifuging and radiation with a week interval between the application of component factors was practically identical to that of centrifuging alone. It is true that spontaneous electric activity of muscles,increased under the influence of acceleration, is significantly reduced on the first day after radiation. However, this reduction does not go beyond the limits of the controls and on the next few days there are wavy fluctuations in electric activity similar to those after centrifuging alone. The average level of electric activity of muscles here is also very high and is not decreased even by the time the animals die.

Thus, the effect of radiation here is practically imperceptible. It is interesting only to note that wave-like changes in myoelectric activity after a combined force are almost always in antiphase to those after centrifuging alone. It is possible that the effect of radiation is, therefore, unique in a combined force: it reduces spontaneous electric activity of muscles on those days when acceleration increases this index and increases it when the level of electric activity is decreased under the influence of centrifuging. The effect of the combined force reliably differs from the control and from radiation
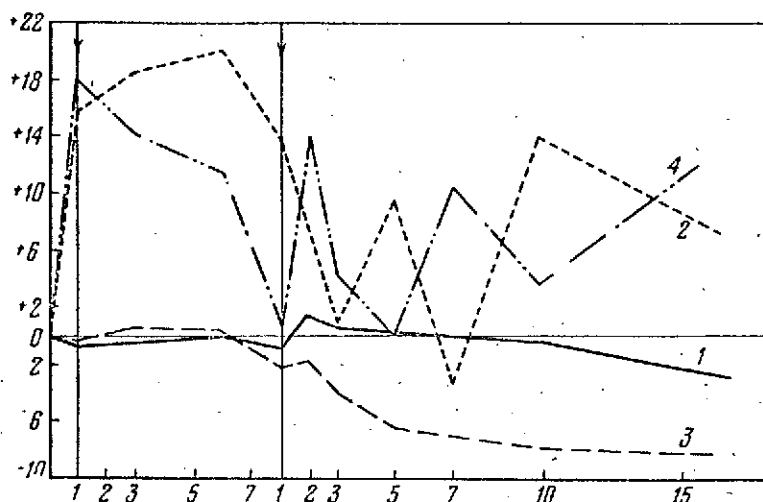
Figure 1. Change in spontaneous electric activity of extensor muscles of the
hind limb of guinea pigs after different kinds of force.

1 — control; 2 — animals exposed to centrifuging; 3 — animals exposed to radiation; 4 — animals exposed to a combined force.

Left arrow — day of centrifuging; right arrow — day of radiation; horizontally —
time after force (days); vertically — integral electric activity of muscles (in
rel. units); zero — average test parameter before force.
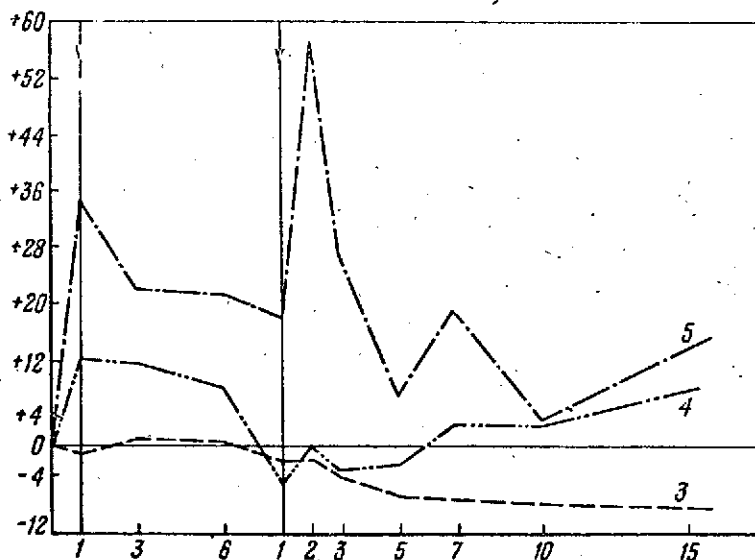


Figure 2. Dependence of changes in spontaneous myoelectric activity after a combined force on initial reaction to preliminary centrifuging.

3 — change in radiated animals; 4 — change after combined force in animals with
a weaker reaction to acceleration; 5 — the same, with a stronger reaction

Remaining symbols same as in Fig. 1.

changes (p<0.001) and does not differ with sufficient reliability from the effect of centrifuging alone (p>0.05).

The degree of influence of preliminary centrifuging on the total effect of the combined force depended (according to this index) on the initial reaction to acceleration. In animals with a clearly pronounced reaction to acceleration (Fig. 2, 5th group), therefore, radiation causes only very slight reduction in spontaneous myoelectric activity the day of radiation. Then a secondary sharp increase in the curve is noted with a subsequent wavy /21 decline. The average level of indices was consistently much higher than in the control and never approached that with radiation alone. In the majority of animals (Fig. 2, 4th group) with a weaker reaction to acceleration, radiation causes much greater reduction in spontaneous electric activity of muscles. On the first day this reduction was even greater than with radiation alone. On the next two days it is reduced, but the effect is, nevertheless, close to that with the isolated force of radiation. Only on the 5th day did the curve representing the effect of the combined force diverge from that representing the results of radiation alone, cross the control level and approach the curve representing changes in the 2nd group. With a weaker response to acceleration, therefore, the effect of subsequent radiation was more marked, although it did not completely cause a summary effect of the combined force.

Myoelectric activity to adequate stimulation of the vestibular apparatus by swinging (Fig. 3) increased after centrifuging and sharply decreased after radiation. The increase in bioelectric activity under the influence of acceleration is maintained for 8-9 days and its reduction under the influence of radiation lasts for the entire examination period. With a combined force the rise in the reaction level, caused by acceleration, was replaced on the first day after radiation by a reduction of vestibulotonic responses. Reduction of myoelectric activity in response to adequate stimulation of the vestibular apparatus also continued later on; however, it was much weaker than with only radiation. Reduction here is replaced by waves of increase and the average level of electric activity is considerably higher than with the isolated force of radiation. Preliminary centrifuging also significantly smoothed out the masking effect of radiation. The curve representing the combined force occupies a middle position between curves representing the effects of radiation alone and

Figure 3. Change in electric activity of extensor muscles of the limb during| /22
adequate stimulation of the vestibular apparatus after different kinds of
force.|

Symbols same as in Fig. 1.

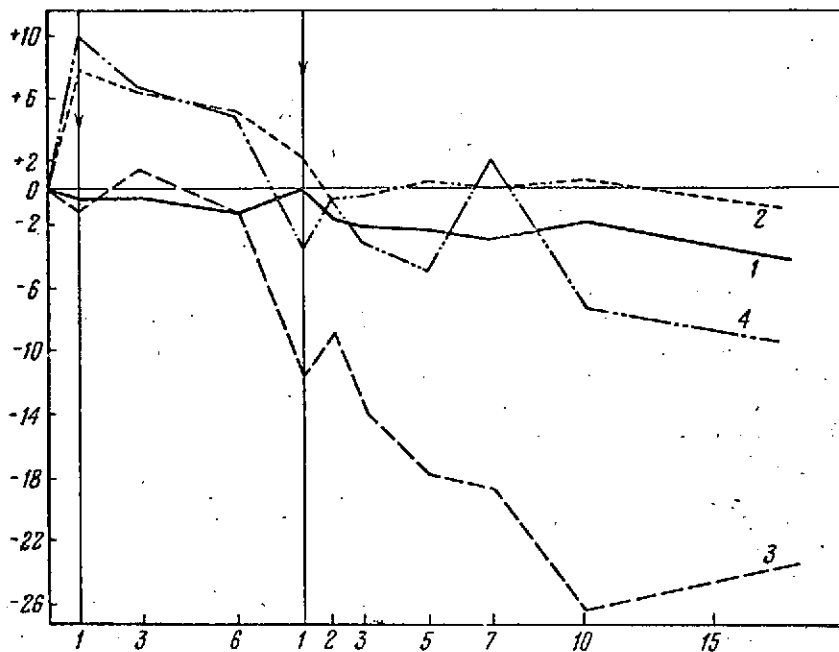Values calculated without respect to spontaneous electric activity of muscles.
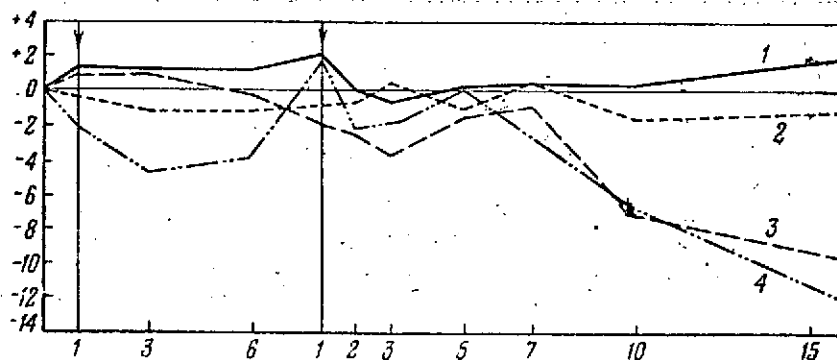


Figure 4. Change in electric activity of extensor muscles of the. limb during|
adequate stimulation of the vestibular apparatus after the isolated and joint
force of acceleration and radiation.

Symbols same as in Fig. 1.

Values calculated without respect to spontaneous electric activity of muscles.

acceleration alone. It is significantely closer to the effect of centrifuging than to that of radiation. Nevertheless, the effect of radiation is seen here both in the direction and in some measure in the shape of the curve of the combined force. Differences from the control and between the effects of tested forces were statistically reliable (from p < 0.05 to p < 0.001).

In calculating the reaction not directly, but in relation to the altered background of electric activity, the ratio between the effects of different forces is less pronounced (Fig. 4). However, here also it can be seen that in the initial period after radiation the curve reflecting the effects of the combined force occupies a middle position between the isolated effects of these factors.

Only on the 7th day did changes in connection with a combined force and /23 with radiation alone become poorly distinguishable from each other.

Very similar relations are also seen in the after-action of the tested vestibulotonic reaction (Fig. 5). Here centrifuging also increases the level of electric activity in the after-action but radiation sharply reduces it. Combined forces give an intermediate effect which is, however, closer to that of acceleration. The degree of the effect of preliminary centrifuging on subsequent postradiation changes depended on the reaction of the organism (according to index data) to acceleration alone (Fig. 6). In the group of animals where reaction to acceleration was strong (Figs. 6, 5) the effect of subsequent radiation appeared weak. The curve representing the effect of a combined force during practically the entire period of examination is located at the level of the curve demonstrating changes after centrifuging alone. The difference between them is not statistically reliable (with reliable difference from the entire group as a whole and from 1 subgroup). Only on the 10th day did the level of after-action in the combined-force group become lower than in the group exposed to acceleration alone. In the same subgroup of animals where reaction to preliminary centrifuging was lower, the effect of radiation appears more quickly and to a greater degree (see Figs. 6, 4). From the first day after radiation, myoelectric activity in after-action is here essentially reduced and during the entire period of the examination remains significantly lower than in the 2nd group. The difference between groups does not even out until the 10th day after radiation.
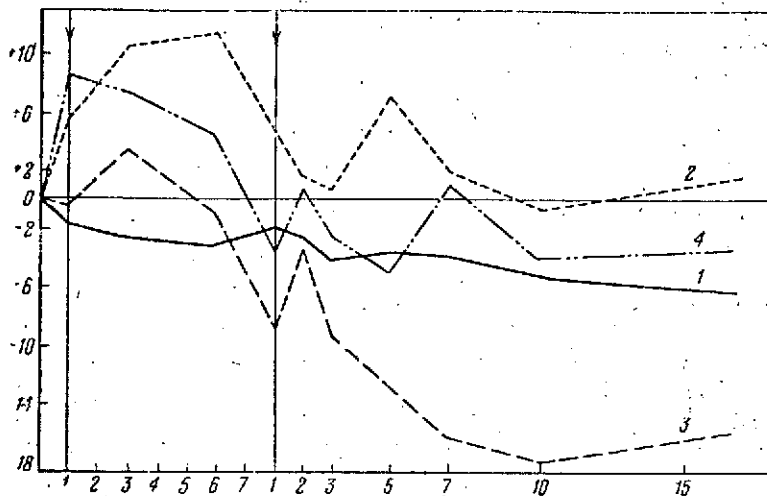
Figure 5. Change in electric activity of muscles in after-action of reaction to
adequate stimulation of the vestibular apparatus after isolated and joint action
of acceleration and radiation.
Symbols same as in Fig. 1.
Values calculated without respect to spontaneous electric activity of these
muscles.
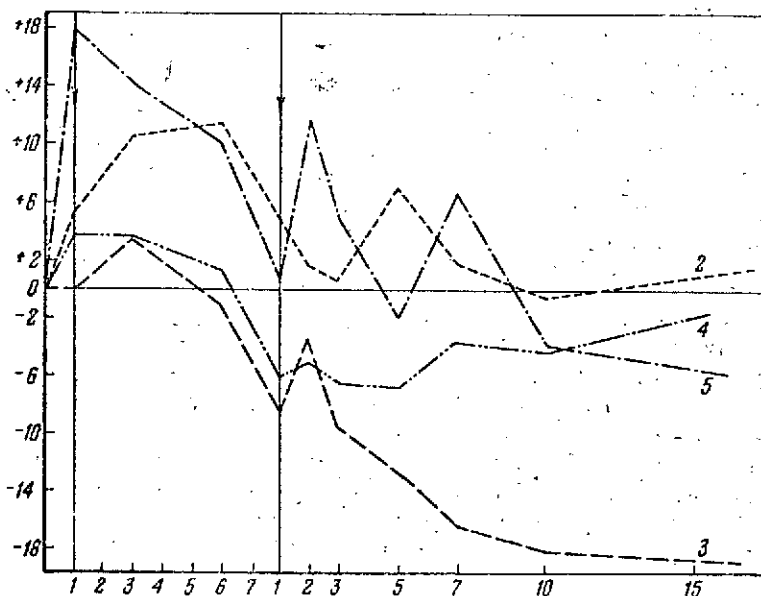


Figure 6. The dependence of changes in electric activity of muscles in after-
action of reaction to stimulation of the vestibular apparatus after a combined
force on the effect of preliminary centrifuging.

2 — change in animals exposed to centrifuging alone; 3 — change in radiated ani-
mals; 4 — change after combined force in animals with weaker reaction to accel-
eration; 5 — the same with a stronger reaction to acceleration.

Remaining symbols same as in Fig. 1.

We must, however, note that the influence of preliminary centrifuging appears essentially in the total effect and in 1 subgroup: the reduction in electric activity in after-action here never reaches such dimensions as with radiation alone. The effect of the combined force in both subgroups reliably differs from the pure radiation effect (p<0.001).

The latent period of bioelectric reaction of muscles to adequate stimulation of the vestibular apparatus (Fig. 7) increases very strongly after radiation but decreases after centrifuging. With a combined force the majority of animals revealed the same changes as with centrifuging alone. The latent period here is even more significantly shortened and is maintained longer than in the group of animals exposed to acceleration alone. The latent period is not essentially lengthened until the tenth day after radiation. However, among animals exposed to a combined force, three guinea pigs showed a completely different type of change in the latent period. Their reaction to preliminary centrifuging was no less (even slightly more) than in all other ani-
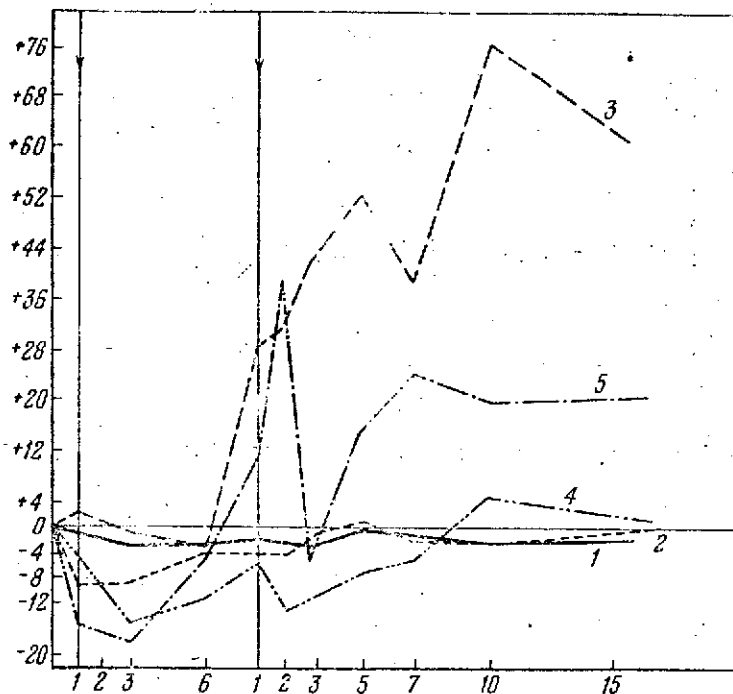
Figure 7. Change in the latent period of electromyographic reaction to adequate stimulation of the vestibular apparatus after isolated and combined action of acceleration and radiation.

4 and 5 — first and second groups of animals exposed to combined action; vertically — duration of the latent period (in rel. units). Other symbols same as in Fig. 1.
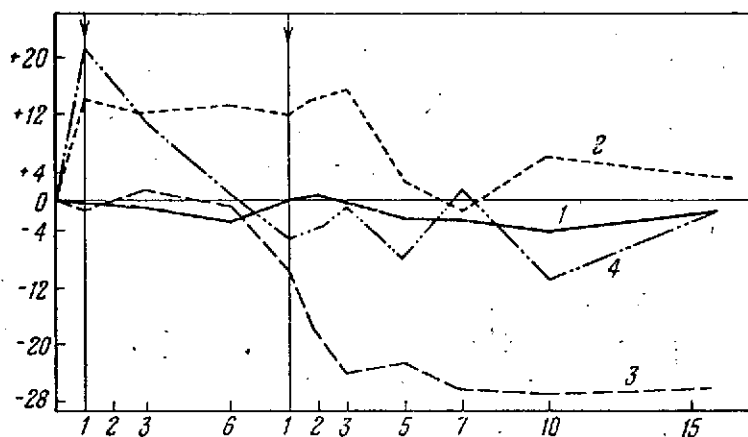
Figure 8.   Change in the duration of the after-action of electromyographic re-| /26
action to adequate stimulation of the vestibular apparatus after isolated and
joint action of acceleration and radiation.

Vertically — duration of after-action (in rel. units).
Symbols same as in Fig. 1.
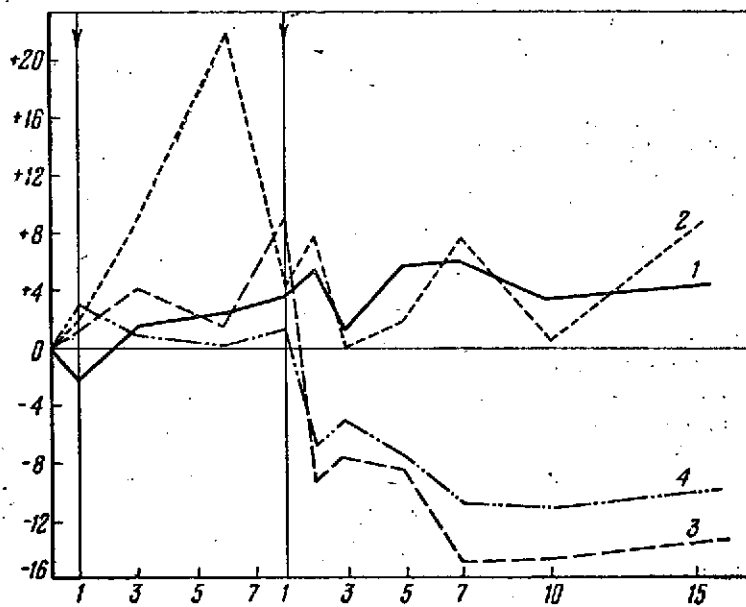


Figure 9.   Change in the number of leukocytes in peripheral blood of animals |
after isolated and joint action of acceleration and radiation.

Vertically — number of leukocytes per 1 mm$^3$ of blood (in % of their average
number before the force and adjusted to the average deviation [for each group]|
from normal before the force).

Symbols same as in Fig. 1.

25

mals; nevertheless, on the first day after radiation their latent period of response to adequate stimulation of the vestibular apparatus was lengthened very significantly. Long latent periods were maintained in these animals during the entire (with the exception of the 3rd day) period of examination. According to this index, therefore, the character of changes in various animals was slightly different: in some the radiation effect was almost completely imperceptible and in others it appeared immediately after radiation. However, in this second group of animals the lengthening of the latent period was also incomparably smaller than with radiation alone. Differences between all examined groups of animals were statistically reliable (from $p<0.05$ to $p<0.001$).

The duration of the after-action of the test reaction (Fig. 8) reveals the same regularity already repeatedly observed in other indices. The effect of the combined force again occupies a middle position between the effects of iso-
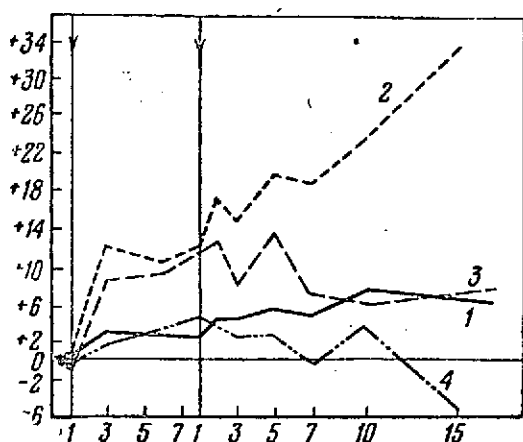
Figure 10. Change in weight of the animals after isolated and joint action of acceleration and radiation.

Vertically — weight (in % of the average weight before the force and adjusted to the average deviation (for each group) from the original level).

Remaining symbols same as in Fig. 1.

lated component factors (again closer to the effect of acceleration).

Centrifuging prolongs the after-action, radiation significantly shortens it and in the case of the joint action of acceleration and radiation the curve of changes (after an initial rise caused by acceleration) is located only slightly lower than the control curve. The effect of the combined force reliably differs from the isolated effect of both acceleration ($p<0.01$) and radiation ($p<0.001$).

All components of the vestibular reflex, therefore, reveal the protective effect of preliminary centrifuging, which partially or even completely reduces

but at any rate masks the effect of subsequent radiation. Clinical indices of the general condition of the animals are a much more complicated matter. It is difficult to make definite conclusions from our data. The number of leukocytes in peripheral blood (Fig. 9) of both groups of animals (exposed to joint action and the action of radiation alone) is reduced almost the same amount. It is true that during the entire period of examination the leukopenia in animals exposed to preliminary centrifuging is slightly lower than in the group of radiated only animals. Differences are statistically unreliable but the tendency toward protection in this series of experiments was, nevertheless, very pronounced. The isolated action of acceleration alone causes leukocytosis, later replaced by wave-like fluctuations at the control level.

Body weight (Fig. 10) of the animals after centrifuging alone was increased as intensively as before the action. It was even slightly more intensive than in the control, which could also be due simply to individual differences in the animals of a given group. In the group of radiated animals (before radiation their body weight increased as quickly as in the group /28 exposed to acceleration only) radiation delayed increment and then also caused a reduction of body weight, although not very sharp. Guinea pigs exposed to the combined action gained weight before radiation with approximately the same intensity as in the control. From the moment of radiation a gradual decrease of body weight begins immediately, most sharply after the 10th day. The protective role of preliminary centrifuging is not revealed here; weight losses in the group exposed to the combined force are approximately the same amount and intensity (even slightly greater) as in the group radiated only. Survival of radiated animals was 22.2±13.7% and in the group exposed to the combined force it was 33.3±13.5%. The difference in our data is not statistically reliable but a tendency toward reduction of mortality was evident in the group exposed to the combined force.

## Results

The results of this work show that centrifuging 7 days before radiation very strongly affects subsequent radiation reactions. This effect is possibly even more significant than with a 3-day interval between the actions [6]. If with a 3-day interval there are practically no differences in the clinical

course and outcome of radiation sickness between radiation alone and a combined force, here there is a clear tendency toward increased survival and reduced changes in the composition of peripheral blood. True, the protective action of acceleration according to this index is not great and in our material statistically unreliable, but it cannot yet be disregarded.

With respect to the characteristics of vestibulotonic reflex, the protective effect of preliminary centrifuging reliably predominates. The effect of the combined force almost everywhere occupies an intermediate position between the effects of component factors; radiation reactions are reduced, sometimes almost completely subordinated by reactions to acceleration (for example, change in the level of spontaneous electric activity). The protective effect against subsequent radiation sometimes depends on the initial level of reactions to centrifuging in given animals: the stronger the response to acceleration, the less was later radiation damage (background electric activity, electric activity in after-action). This was the first time such a phenomenon was noted; it was not observed in earlier series of experiments.

Myoelectric activity during adequate stimulation of the vestibular apparatus usually changes less during these actions than spontaneous electric activity of muscles in a state of relative rest. Therefore, in expressing reaction and /29 its after-action as the ratio between electric activity of muscles during stimulation of the vestibular apparatus and increased background activity, differences between different kinds of forces are slightly evened out and become less demonstrative. It is possible that lower susceptibility is caused biologically: maintenance of a certain level of response to adequate stimulation should ensure normal existence of the organism in changing environmental conditions.

The latent period and the length of the after-action of vestibulotonic reaction sometimes change variously in different animals exposed to the same force (divided into subgroups). Evidently these parameters of myotonic reflex are most sensitive and are more subject to individual and other fluctuations.

We must also note that after a combined force test animals very often die when indices of the vestibulotonic reflex are normal. The protective effect of preliminary centrifuging on postradiation changes in the vestibulotonic reflex (observed in these experiments) completely agrees with recent literature data. The protective role of dynamic forces can, evidently, be considered

universally recognized. Mechanisms of this protection, however, are still far from clear. We have already discussed the possible value of hypoxia and related increased activity of the hypophysis-cortical link of the neuroendocrine regulation system (according to literature data) in a preceding work [6]. We also noted there the importance of the level of activity of the central nervous system, its plasticity and other functional characteristics. In addition, a definite role can also be played in reactions of the vestibular analysor by the functional interaction of cupular and otolithic apparatus during accelerations. The correlation between reactions of these systems and acceleration varies and involves change in the reactivity of the organ of balance and its sensitivity to various forces [20, 21, 24].

The influence of the dynamic factor on the radiation effect depends not only on parameters of the forces, but also on the interval of time between them. There is still very little literature data on this question and they are slightly contradictory as is always the case in the beginning of solving a certain problem. Studies most often were conducted on rats and mice; the interval between forces did not usually exceed several hours or a few days [1, 2, 8]. However, with such intervals there were also already indications of the possibility of increasing the protective effect of the dynamic force by increasing the time before subsequent radiation [22, 26].

In the pathomorphological work of a group of authors [7] it was established that vibration (70 cps, 0.54 mm) three and especially one day before radiation (700 r) increased the devastation of follicles of the spleen and /30 lymphocyte impoverishment. When radiation was combined with preliminary vibrations bone marrow was damaged less than with radiation alone. But here, vibration three days before radiation also influenced the radiation effect less than vibration one day before. The recovery of all kinds of hematogenesis in the spleen and bone marrow was accelerated with the combined force. Overloads (10 g, 30 min.) one day before gamma-radiation reduced the devastation of follicles of the spleen and accelerated recovery of hematogenesis.

T. S. L'vova [16] established that vibration (70 cps for one hour) 1.4 and 24 hours before radiation in doses of 450, 600 and 1300 rad reduces the mortality of mice 10-20% and increases the length of life 10-40%. Such vibration 5 days before radiation increased the mortality of mice and shortened

the average length of life. The author feels that there is usually a protective effect of vibration only when the interval between forces does not exceed 24 hours.

With various combinations of radiation, linear accelerations and vibration [25] there was protection and increased damage as well as lack of any interaction between factors, depending on the value, dose rate and interval between forces.

The importance of the time interval between component factors in a combined force, therefore, is undoubted, although studies on this question are still very few. In existing works, increasing the time between forces to 3-5 days usually reduced the effectiveness of the dynamic factor on radiation reactions. No studies with a longer interval between forces are known to us. These experiments did not reveal the expected reduction of radiation reactions due to preceding | acceleration when the interval between forces was increased from 3 to 7 days. Rather, there was even a slight increase of this effect. To a certain degree this can be connected with species characteristics of guinea pigs whose sensitivity to accelerations differs in several respects [19]. However, most important here, evidently, is the complexity of the interference between component factors with different kinds of combined force. It is extremely probable that the effect of the dynamic stimulus on radiation effects does not simply subside when the time between forces is increased. Evidently, there is a certain optimum interval when this stimulus is most effective. It is very possible that the interval between centrifuging and radiation which we used is also the optimum or close to optimum for this| force. The assumption is all the more probable that data exist on increased resistance of rats to physical loads precisely 7 days after centrifuging. It may be in- /31 ferred that the optimum effect of the dynamic force does not always correspond to a short time interval, sometimes it is also possible with a relatively long period. In addition, the presence of two or even several optimum periods of time for the most effective influence of the dynamic force on subsequent radiation reaction is not ruled out. The change in acute and remote radiation effects under the influence of dynamic factors can have a completely opposite direction. Discovering regularities in the mutual effect of factors and the dependence of this effect on the time interval between forces is important not

only theoretically, but also for space flights. Optimum or minimum effectiveness of preliminary dynamic factors can change the degree of radiation danger in flight and affect the ability to work of the crew. This problem is complex and varied; its solution requires numerous special studies.

## Conclusions

1. Preliminary centrifuging ($-8g_x$, 15 min.) 7 days before radiation (500 r, 169 r/min.) essentially alters the effect of radiation on the functions of the vestibular analysor.

2. With the indicated combined force the protective effect of the dynamic factor on subsequent effects predominates. Postradiation changes are significantly decreased and sometimes completely masked by the effects of acceleration even up until death of the test animals. There are also more complicated cases of interaction between component factors: different effects in different animals with the same force, in a combined effect repetition of the dynamics of one factor with predominance of the direction of the other, etc.

3. In some cases it is possible to trace the relation between the initial level of the reaction to centrifuging and the subsequent effect of acceleration on radiation reactions.

4. The effect of preliminary centrifuging on the clinical course of radiation sickness and survival of animals was statistically unreliable in the data of this study. Nevertheless, with a combined force there was a pronounced tendency toward improvement of survival and reduction of changes in peripheral blood.

5. Comparison of data of this and preceding [6] works shows no reduction in the effectiveness of the dynamic factor on radiation effects when time between forces is increased from 3 to 7 days. Even some increase in effectiveness can be noted.

## REFERENCES

1.  Arsen'yeva, M.A., L.A. Belyayeva and A.V. Golovkina. In the book: "Prob- /32
    lemy kosmicheskoy biologii" (Problems of Space Biology). Moscow, "Nauka",
    Vol. 4, 1965, p. 373.

2.  Arsen'yeva, M.A., L.A. Belyayeva, Yu.S. Demin, G.L. Pokrovskaya, A.V.
    Golovkina and L.I. Gavrilina. Kosmicheskiye issledovaniya, Vol. 3, No.
    5, 1965, p. 796.

3.  Arsen'yeva, M.A., V.V. Antipov, L.A. Belyayeva and A.V. Golovkina. In
    the book: "Problemy kosmicheskoy meditsiny" (Problems of Space Medicine),
    Moscow, 1966, p. 39.

4.  Apanasenko, Z.I. In the book: "Vliyaniye ioniziruyushchikh izlucheniy
    i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy"
    (The Effect of Ionizing Radiations and Dynamic Factors on Functions
    of the Central Nervous System). Moscow, "Nauka", 1964, p. 92.

5.  Apanasenko, Z.I. In the book: "Vliyaniye faktorov kosmicheskogo poleta
    na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight
    Factors on Functions of the Central Nervous System). Moscow, "Nauka",
    1966, p. 218.

6.  Apanasenko, Z.I. In the book: "Nekotorye voprosy kosmicheskoy neyro-
    fiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka",
    1967, p. 184.

7.  Gaydamakin, N.A., V.G. Petrukhin, V.V. Antipov, P.P. Saksonov and V.S.
    Shashkov. Izv. AN SSSR, Biology series, Vol. 3, 1966, p. 346.

8.  Davydov, B.I., V.V. Antipov, N.I. Konnova and P.P. Saksonov. Kosmicheskiye
    issledovaniya, Vol. 3, No. 5, 1965, p. 789.

9.  Zharova, Ye.I., S.A. Khrustalev, T.G. Protasova, B.I. Davydov, V.V.
    Antipov, P.P. Saksonov and M.O. Raushenbakh. Izv. AN SSSR, Biology
    series, Vol. 2, 1967, p. 290.

10. Ivanov, K.V., M.V. Zhukov and M.G. Molchanova. Patologicheskaya fiziologiya
    i eksperimental'naya terapiya, Vol. 6, No. 5, 1962, p. 74.

11. Kuznetsova, M.A. In the book: "Vliyaniye ioniziruyushchikh izlucheniy
    i dianamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy"
    (The Effect of Ionizing Radiations and Dynamic Factors on Functions
    of the Central Nervous System). Moscow, "Nauka", 1964, p. 122.

12. Lazar', A.F. In the book: "Voprosy patologii fiziologii" (Questions of
    Pathology of Physiology). Kiev, Gosmedizdat UkSSR, 1963, p. 170.

13. Livshits, N.N.,and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov kos-
    micheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect
    of Space Flight Factors on Functions of the Central Nervous System).
    Moscow, "Nauka", 1966, p. 236.

14. Livshits, N.N., Z.I. Apanasenko and Ye.S. Meyzerov. Radiobiologiya,
    Vol. 9, No. 1, 1969, p. 46.

32

15.  Luk'yanova, L.D.  In the book:  "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System).  Moscow, "Nauka", 1964, p. 145.

16.  L'vova, T.S.  Izv. AN SSSR, Biology series, Vol. 3, 1966, p. 355.

17.  Nesterenko, V.S.  Radiobiologiya, Vol. 4, No. 4, 1964, p. 643.

18.  Parfenov, G.N.  Kosmicheskiye issledovaniya, Vol. III, No. 4, 1965, p. 643.

19.  Sirotinin, N.N.  Patologicheskaya fiziologiya i eksperimental'naya terapiya, Vol. 5, No. 5, 1961, p. 13.

20.  Yuganov, Ye.M. and A.I. Gorshkov.  Izv. AN SSSR, Biology series, Vol. 6, 1966, p. 816.

21.  Yuganov, Ye.M. and A.I. Gorshkov.  In the collection:  "Fiziologiya vestibulyarnogo analizatora" (Physiology of the Vestibular Analysor), Moscow, "Nauka", 1968, p. 89.

22.  David, H.M.  Missiles and Rockets, Vol. 10, No. 17, 1963, p. 22.

23.  Lyle, J.M.  Aerospace Medicine, Vol. 32, No. 6, 1961, p. 563.

24.  Melvill, J.G.  Journal of Laryngology and Otology, Vol. 80, No. 3, 1966, p. 207.

25.  Musgrove, W.S. and E.B. Sprague.  Nuclear Science, abstracts, Vol. 21, No. 6, 1967, p. 947.

26.  Zellmer, R.W., G.J. Womack, R.C. McNee and R.G. Allen.  Aerospace Medicine, Vol. 34, No. 7, 1963, p. 626.

27.  Wolf, S. and R.C. Borstell.  Proc. Nat. Acad. Sci., Vol. 40, No. 12, 1954, p. 1138.

# THE EFFECT OF BRIEF PRELIMINARY CENTRIFUGING AND ACUTE GAMMA RADIATION
## ON THE STATE OF THE VESTIBULOTONIC REFLEX WITH A
### WEEK INTERVAL BETWEEN FORCES

Z. I. Apanasenko

Results of earlier works showed that the effect of centrifuging is quite prolonged and its subsequent effect on radiation changes in the system of the vestibular analysor is also clear when there is a significant interval between the forces (see this collection). As all previously used accelerations were relatively long (15 min.), there has been interest in studying the action of shorter accelerations and tracing their influence on subsequent radiation effects.

The study was conducted under conditions practically identical to those of preceding works. Only the value of acceleration and its length were changed. Experiments in this series showed that reducing the time of preliminary centrifuging from 15 to 4 minutes (with simultaneous increase of acceleration from — 8 to — 10 g) does not eliminate and even does not reduce its modifying influence on radiation effects. Total radiation of guinea pigs in a dose of 500 r after preliminary (7 days) centrifuging causes changes completely different from those after radiation alone in the same dosage and under the same other conditions. As in the other earlier experiments, the influence of acceleration in a combined force very often comes to the foreground and masks radiation damage. This was strikingly evident in the change in background spontaneous electric activity of the tested muscles (Fig. 1). Here two groups of animals (a group exposed only to centrifuging and a group which was radiated with a dose of 500 r 7 days after centrifuging) reveal practically identical reactions to acceleration. Spontaneous bioelectric activity of muscles sharply increases. This increase is the same in both groups of animals and is maintained for the same time (9 days) after the force. However, it is especially interesting that according to this index after radiation the animals exposed to the combined force are practically the
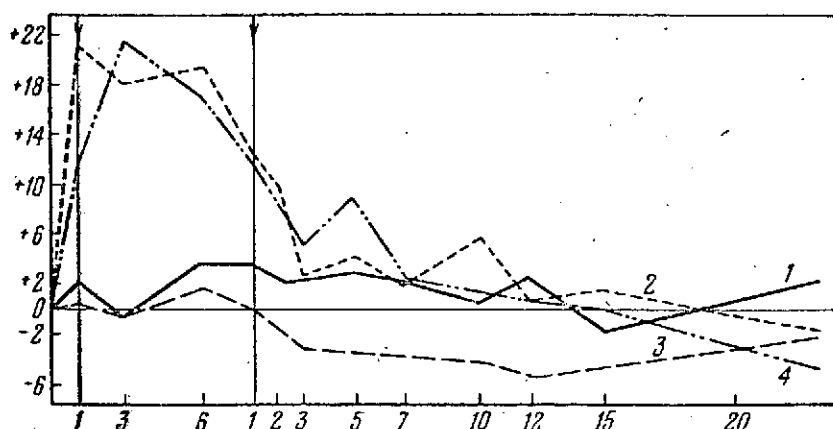
Figure 1. Change in spontaneous electric activity of extensor muscles of the| /34
hind limb of guinea pigs after different kinds of force.

1 — control; 2 — isolated action of centrifuging; 3 — isolated action of radiation; 4 — combined action of centrifuging and radiation. Left arrow — day of centrifuging; right arrow — day of radiation; horizontally — time after force (days); vertically — integral electric activity of muscles (in rel. units); zero — average test parameter.

same as those exposed to centrifuging alone. Curves demonstrating changes in both groups undulate, gradually approach the level of the control and are later practically the same. Only on the 20th day, even after death of half the animals, background electric activity of muscles in guinea pigs exposed to the combined force is below the control and approaches that in radiated animals. It is natural that statistical analysis of the results by the median test reveals no differences between the combined force and the action of acceleration alone. Divergence from the control is statistically reliable (p<0.01). Changes caused by radiation alone also reliably differ from the control (p<0.05). By the second day after radiation spontaneous electric activity of muscles is already reduced and remains below the level of the control during the entire examination period. The reduction in amplitude is not very great,|but it is stable and of the same type for all animals in the group. According to this index, therefore, radiation changes are completely imperceptible in the group exposed to the combined force, where externally they seemed to be eliminated by preliminary centrifuging.

Vestibulotonic reaction to adequate stimulation by swinging was not

changed in the test groups of animals in the same direction as background
activity (Fig. 2.). Radiation causes a gradual reduction in the level of
the reaction and centrifuging increases it. A level above that of the con-
trol is maintained until the 10th day after the control trip to the radiation
site, i.e. until the 17th day after centrifuging. Radiation after preliminary
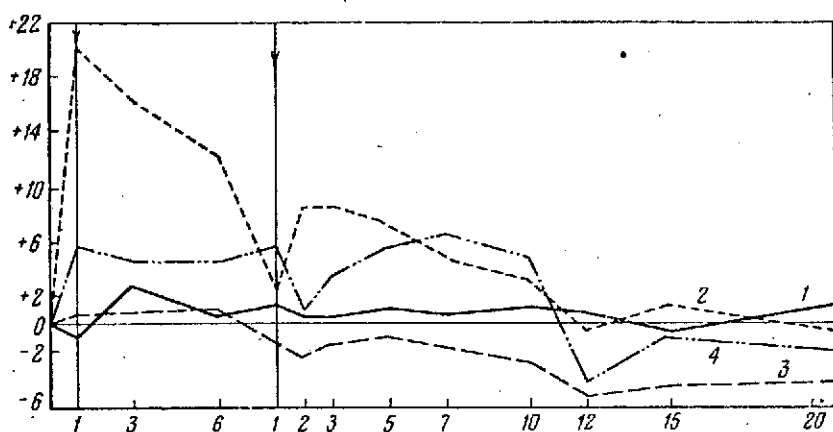
Figure 2. Change in electric activity of extensor muscles of the limb during
adequate stimulation of the vestibular apparatus after different kinds of force.
Symbols same as in Fig. 1.
Values calculated without respect to spontaneous electric activity of muscles.
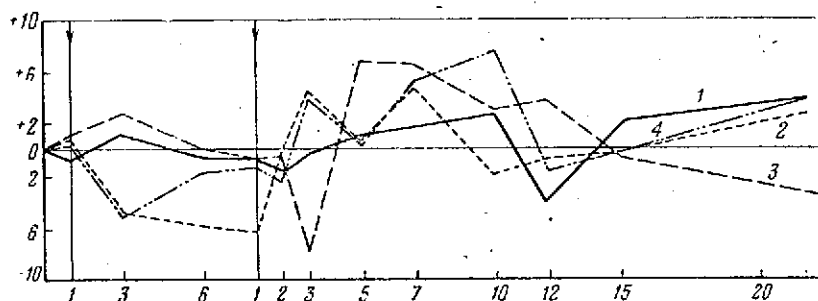


Figure 3. Change in electric activity of extensor muscles of the limb during
adequate stimulation of vestibular apparatus after isolated and joint action
of acceleration and radiation.
Symbols same as in Fig. 1.
Values calculated without respect to spontaneous electric activity of these
muscles.

acceleration did not reduce vestibulotonic reaction to the control level until the second day. Then again there is an increased reaction, the same as in animals exposed to centrifuging alone. The curve reflecting results of the combined force did not diverge from that demonstrating changes after centrifuging until the 12th day after radiation and assume a middle position between it and the curve of changes from radiation alone. Thus, radiation changes of vestibulotonic reaction are also significantly masked by preliminary centrifuging. Changes shown by this index are significantly lower than those revealed by spontaneous electric activity, but the effect of centrifuging in groups of animals exposed to acceleration alone and a combined force is different.

Figure 4. Change in electric activity of muscles in after-action of reaction to adequate stimulation of the vestibular apparatus after isolated and joint action of acceleration and radiation.
Symbols same as in Fig. 1.
Values calculated without respect to spontaneous electric activity of muscles.
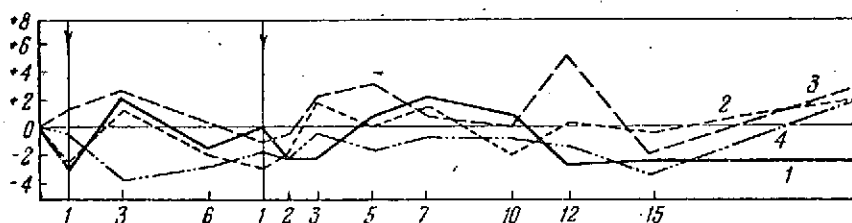


Figure 5. Change in electric activity of muscles in after-action of reaction to adequate stimulation of vestibular apparatus after different kinds of force.
Symbols same as in Fig. 1.
Values calculated in relation to spontaneous electric activity of these muscles.
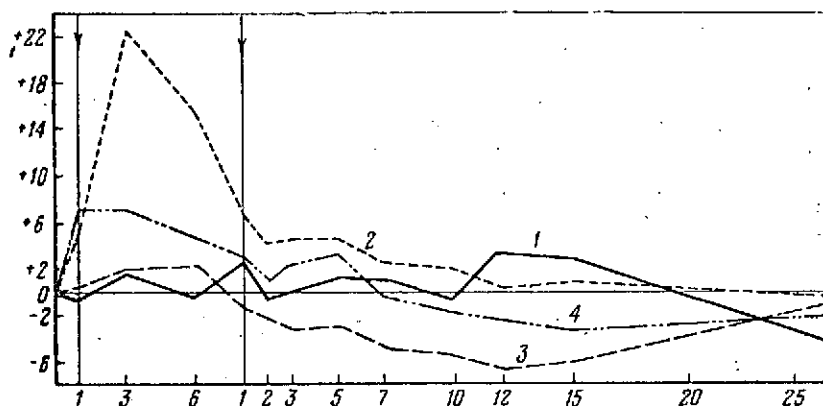
Nevertheless, the character of the isolated and joint effect of the factors is quite clear. Differences between all four experimental groups of animals are statistically reliable (from p<0.05 to p<0.01). When the reaction is expressed in percent of spontaneous electric activity of these same muscles (Fig. 3) the difference between groups is evened out; the general picture is less clear, although here the curve of results of a combined force is usually located closer to the curve of centrifuging effects rather than the curve of radiation changes.

The after-action of vestibulotonic reaction to swinging (Fig. 4) is sharply increased after centrifuging and quite significantly reduced after radiation. Reaction to preliminary centrifuging in animals exposed to a combined force was weaker than in animals exposed to acceleration alone, however, it also significantly affected the later course of changes after radiation. Until the 7th day practically no radiation effect was evident. Only after the 10th day did the reduction of electric activity in the after-action become

Figure 6. Change in the latent period of electromyographic reaction to stimu-lation of the vestibular apparatus after isolated and joint force of acceleration and radiation.

Vertically — the latent period (in rel. units).

Other symbols same as in Fig. 1.

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marked and the curve move closer to that reflecting the result of radiation alone. According to this index, the combined force occupies the typical intermediate position between the effects of isolated component factors. Differences between all four groups of animals are statistically reliable (p<0.05; p<0.001).

When electric activity of after-action is related to decreasing (after the force) spontaneous electric activity, the difference between groups (as noted according to the previous index) is reduced and curves of changes in all groups converge (Fig. 5). Nevertheless, here also the effect of the combined force differs much more from the effect of radiation (p<0.05) than from that of acceleration (p>0.05).

The latent period of vestibulotonic reaction to adequate stimulation of the vestibular apparatus (Fig. 6) changes after each of the forces very significantly. After radiation it immediately increases sharply. The increased length of the latent period continues throughout the entire period of examination until death of the animals. Centrifuging shortens the latent period of the reaction, which is maintained to the 7-10th day after the control trip to the radiation site, i.e. for 14-17 days after acceleration. Later the latent period converges with that in the control. In animals exposed to a combined force, practically the same reduction in the latent period is maintained only until the 5-7th day after radiation (12 days after centrifuging). After the 7th day radiation changes are no longer masked by preceding acceleration and appear in the form of a sharp increase in the latent period of the reaction. Changes in the combined group from this point parallel those in the group exposed to regular radiation. The effect of the combined force reliably differs both from the control and from the isolated effect of acceleration or radiation (p<0.001).

Similar relationships hold for another test - the duration of action of the vestibulotonic reaction studied (Fig. 7). Here acceleration increases the duration of the after-action, and radiation greatly shortens it. In the case of composite action, preliminary centrifuging decreases the after-action duration and makes it less pronounced than with single radiation. Only at the 12th day after radiation, before the death of the majority of animals, the curve for composite action converges with the radiation curve. Up until this time, it occupies a middle position between the effects of isolated action. Change in all groups of experimental animals differ from the control and from each other (p<0.01 or p<0.001).

Thus, based on all characteristics of vestibulotonic reflexes, preliminary centrifuging emerges as a powerful modifying factor, strongly changing the later course of radiation reactions.
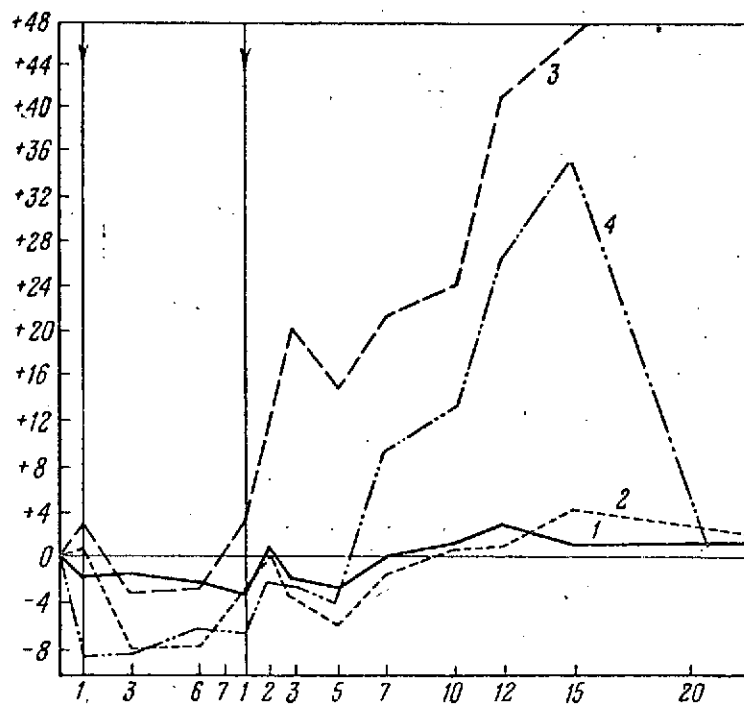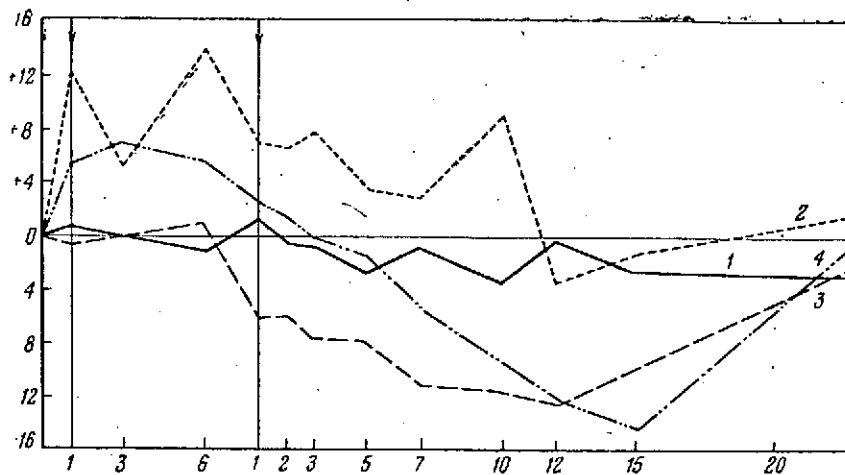


Figure 7. Change in the length of after-action of the electromyographic reaction|/39 to adequate stimulation of the vestibular apparatus after isolated and joint forces of acceleration and radiation.

Vertically — length of after-action (in rel. units).

Other symbols same as in Fig. 1.
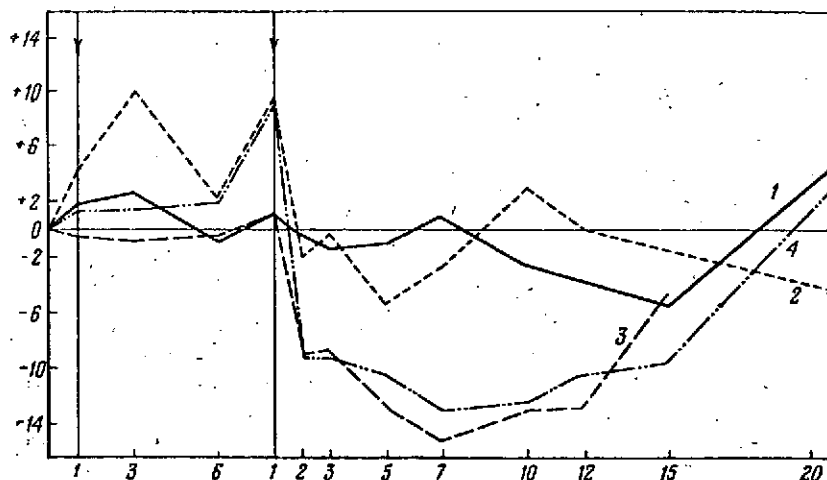


Figure 8. Change in the number of leukocytes in peripheral blood of animals| after isolated and joint force of acceleration and radiation.

Vertically — number of leukocytes in 1 $mm^3$ of blood (in % of their average number before the force and adjusted to the average deviation (for each group) from normal).

Other symbols same as in Fig. 1.

After radiation hematological changes are subject to the influence of preliminary centrifuging only to a very small degree. Similar insignificant protections occur here only in some cases; usually radiation changes in hematological indices in the group exposed to a combined force are analogous to those in the group radiated only. Fig. 8, therefore, gives changes in the number of leukocytes after different kinds of forces. Centrifuging causes leukocytosis, giving way by the 9th day to wave-like fluctuations at the control level. After radiation leukopenia is strongly evident by the 2nd day and later is aggravated even more. Restoration of the leukocyte content in surviving animals usually begins on the 10-12th day. With a combined force, leukocytosis caused by centrifuging is changed to leukopenia as rapidly as with radiation alone. The severity of leukopenia in both groups was approximately the same ($p > 0.05$). Differences between the control group and that subjected to centrifuging alone are statistically reliable ($p < 0.01$). Survival in the group of radiated animals was 27.3% and among animals exposed to a combined force it was 50%. This difference was statistically unreliable in our data but a tendency toward reduction of postradiation mortality of animals under the influence of preliminary acceleration was clear.

This series of experiments, therefore, shows some protective effect of preliminary centrifuging according to the index of animal survival in the absence of an index on number of leukocytes in peripheral blood.

As in previous works, the effect of penetrating radiation on the vestibulotonic system is very largely determined by the preliminary force of acceleration. The effect of brief tenfold overload on subsequent radiation reactions does not essentially differ from already-known (from earlier works) regularities in the interaction between radiation and longer eight-fold overload. In the effect of the combined force the dynamic factor also usually predominates, masking the reaction to radiation, often up until death of the animals. The effect of a combined force also occupies an intermediate position between the effects of isolated component factors and the direction of one of the factors is combined with the dynamic effect of the other, etc. Change in the parameters of the dynamic force under our conditions, therefore, entailed a significant change in its influence on the effect of later radiation. Discussion of the regularities and possible mechanisms of such an influence, presented in

the preceding | work in this collection, as a whole also applies to the results of this series of experiments. More essential for the specifics of the combined force of acceleration and radiation is, evidently, change in the very character of the dynamic factor and the time between centrifuging and radiation. Study of this question should be the subject of future experiments.

# A COMPARISON OF THE ISOLATED AND COMBINED
## ACTION OF VIBRATION AND IONIZING RADIATIONS
## ON CONDITIONED REFLEXES AND MAZE LEARNING| IN RATS

N. N. Livshits, Ye. S. Meyzerov,
R. M. Zakirova, V. A. Tikhaya

Previously studying the combined action of vibration and fractionated | /41 |
x-rays on conditioned-reflex activity of rats, we found that first the combined
force caused an effect similar to vibration. After the second and third ex-
posures a sharp increase was observed in the radiation effect throughout the
entire period of observations [7]. The predominance of the effect of the
dynamic factor in various forms | in cases of combined forces of radiations
and vibrations has been described repeatedly [1, 8, 9], but the second step
in the reaction — complete and prolonged summation of the effects of combined|
forces — has been recorded in only two cases.*

In 1966-1967 Ye. M. Skobeyev studied the effect of these forces on maze
learning [11, 12, 13]. He found no reliable increase in radiation effect in
rats exposed to preliminary vibration. In his tests the deterioration of
indices of maze learning after isolated forces of radiations and vibration
was much less pronounced than in our test [7], in which the conditioned re-
flexes method was used.

Differences in the results could have been due to lack of perfectly
identical tests in both studies. Preliminary preparation of animals in con-
ditioned reflex tests took 8 months and the development of maze learning about
2 weeks; although to equalize conditions Ye. M. Skobeyev began preparation of
the animals at a slightly later age than N. N. Livshits and Ye. S. Mayzerov,
in the second of these studies the rats were 3-4 months older during the time
of exposure to the forces than in the first work.

Maze tests were conducted 4 times a week after the forces and 3 times a
week the rest of the time but conditioned reflex tests were conducted daily,

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* See discussion in next article in this collection.

except holidays. The latter could play an important role; as is known, in the laboratories of I. P. Pavlov 1-3 day tests were used as a therapeutic means in treating disturbances of higher nervous activity in dogs. Differences in food excitability of the animals could also be important. Feed was taken away from the rats 4 hours before the conditioned reflex tests and 18-20 hours before the maze tests. In the latter case only milk and vegetables remained in the cages.

For these reasons in preparing his works for publication, Ye. M. Skobeyev /42 refrained from comparing the effect of these forces on maze learning and conditioned reflexes, feeling this the subject for a future study. Such a comparison is important for evaluating the effect of radiation and dynamic factors on different kinds of higher nervous activity.

From the literature it is known that certain signs of deterioration of conditioned reflex activity are observed after comparatively small doses of radiation. Individual authors have described the unfavorable effect on conditioned reflexes of radiation in doses of several roentgens [3, 4]. Deterioration of conditioned reflex activity after radiations in doses of 150 r is found in three works [5]. At the same time, no deterioration of maze learning was found with radiation in significantly higher doses [14 and others].

We expressed the opinion that existing differences were due not to errors of the researchers, but to characteristics of the methods.* The conditioned reflex method detects disturbances of higher nervous activity better but the maze method is better for compensatory processes. This is because in learning a maze skill the animal uses information received through various analysors as well as various effector systems, creating the most favorable conditions for compensation [4, 5]. We proceeded from the well-known opinion of I. P. Pavlov that the above-noted characteristics of the maze method offer more possibilities for detecting compensation of surgical damage to the cortex [10]. From our point of view the maze method has even greater possibilities for studying compensation of radiation injuries which are focal-diffuse in nature. As noted above, we also detected these differences in studying the action of vibration as well as the combined forces of vibration and radiations on conditioned reflexes and maze learning, which could also be explained the

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*The history of the question has been dealt with in detail in our publication [5].

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same as differences in the effect of radiation.  To prove this theory it was necessary to compare the action of radiation, vibration and a combination of these factors on conditioned reflexes and maze learning under identical conditions.  That was the purpose of this part of the study.

## Technique

In order to compare the action of these factors on conditioned reflexes and maze learning, we made a study of the effect of these forces on conditioned reflex activity of rats under methodological conditions as identical as possible to those used by Ye. M. Skobeyev to study the effect of these factors on maze learning.   <span>/43</span>

Tests were conducted on white male Wistar rats.

In the work we used a modified chamber for studying conditioned reflexes similar to the one described by the authors of [2].  On the suggestion of engineer V. P. Kornil'yev in the design of the unit the electrodynamic counter was replaced by electronic millisecond timers and integrators.

Latent periods and the strength of conditioned reflexes were recorded. The latter were expressed as the product of the average amplitude of movement of the door and the length it is open during a conditioned stimulus.  This value was determined in arbitrary units by means of an electronic integrator. The conditioned reflex stereotype included eight stimuli, applied in the following order:

1) feeding (without a conditioned signal),

2) Tone with a frequency of 800 Hz (Tone +),

3) Light (flashing a secondary bulb of the same power as bulbs used to illuminate the chamber),

4) Light,

5) Tone +

6) Tone — 400 Hz (Tone —),

7) Tone +,

8) Light.

Five seconds after activating Tone + and the light the rats were given sunflower seeds (the seeds were also used for feed in the maze).  Tone — served as differentiation.  The stereotype we used was not complicated.  It is ex-

tremely difficult to select a conditioned reflex stereotype and maze learning of identical complexity and the very possibility of solving this problem is doubtful. We used one of the simplest stereotypes used by Soviet researchers to detect the action of radiation on higher nervous activity. The maze used in the tests of Ye. M. Skobeyev is a comparatively simple one (See Fig. 1 in the next| article). However, it was somewhat more complicated than maze III of Leshki, used to detect the effect of radiations during the antenatal period on maze learning [16]. Therefore, we feel it is acceptable to compare results of the  tests, obtained by these methods.

A conditioned reflex to Tone + (200 associations with food) was developed and firmly fixed in the rats. Differentiation was exhibited about 30 times and by the start of the forces its development was not yet complete. Light was introduced into the stereotype only the day before the first force. (In tests of Ye. M. Skobeyev the forces were also begun before termination of the development of maze learning). Tests were conducted 3 times a week, but during the time the forces were being applied immediately after exposures and the next day, and then as usual. Feed was removed 18-20 hours before the test /44 and at that time only milk and vegetables remained in the cages. Test and control rats were kept together in groups of 15 in large common cages.

Preliminary preparation of the animals took a total of 2½ months. At the start of development of the conditioned reflex stereotype the rats weighed 200-300 g and by the time the forces were started reached 320-400 g. A total of 29 rats were used in the tests, divided into four groups. Taken into account in distributing the rats among the groups were indices of their higher nervous activity during preliminary preparation; rats were divided so that the size of the groups was as equal as possible.

1. The control group (6 rats) — while the test rats were undergoing vibration they were kept in the same kind of boxes as the test animals near the operating vibrostand and then transferred to the control desk in the x-ray room, but exposed to no forces.

2. This group (7 rats) was exposed to general vertical vibration (70 cps, amplitude 0.4 mm, 15 min.). Vibration was accompanied by noise of about 75 db.

3. This group (8 rats) was kept in the vibrostand (off) for 15 minutes,

and then immediately exposed to general x-ray radiation in a dose of 50 r under the following conditions: RUP-200 unit, 190 kv, filters: copper 0.5 mm + aluminum 0.75 mm, skin-focal length (to the center of the body) 49 cm, dose rate 31 r/min.

4. This group (8 rats) was exposed to vibration and promptly to radiation under the same conditions and in the same dosage as the third group.

The vibrostand, the x-ray room and the unit for studying conditioned reflexes were located in the same building and tranporting the rats to each of these locations took only several minutes.

The forces were supplied three times. They were begun on Aug. 20 and ended Sept. 10. The interval between the first and second forces was 14 days and between the second and third 7 days. In addition to studies of conditioned reflex activity, observations were made of weight and the clinical condition of the rats. The number of leukocytes in peripheral blood was studied at the same time in other groups of rats exposed to the same forces. Rats used for hematological studies were of the same age as those in the main group, they were weaned at the same time and kept under identical conditions.

Results of the experiments were subjected to statistical analysis by the median criterion and in individual cases by Student's criterion.

<center>Results of studies</center> <span style="float:right">/45</span>

During the entire period the rats were exposed to the forces they were bright and active. The weight of rats exposed to radiations decreased an average of 15 g and that of controls during the same time 12 g. Differences between changes in weight of test and control animals were very slight and statistically unreliable. The weight reduction during the forces was probably due to a longer period of food deprivation on days when the forces were applied.

The total number of leukocytes was decreased in rats exposed to radiations and combined forces. No differences in leukopenic reaction were noted between these groups (Fig. 1). The conditioned reflex activity of our rats had not been stabilized before the forces were applied.

During the time when the first and second forces were supplied the strength of the conditioned reflex to Tone + in control animals increased,

which was also observed in radiated animals. To level out the small difference in the initial background of compared goups, we expressed the strength of the conditioned reflex to Tone + in percentages of the initial level and then subjected them to statistical analysis. Such an operation was justified as the median criterion is nonparametric.
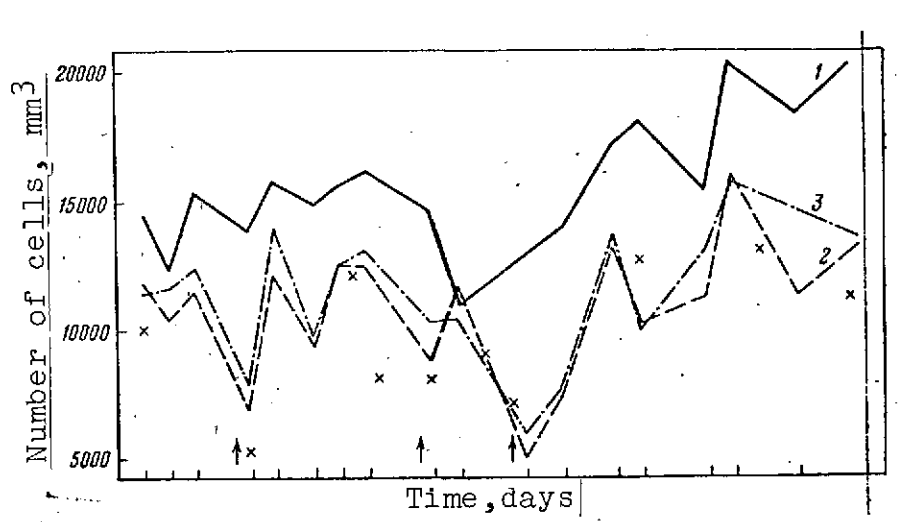


Figure 1. The effect of radiations in single doses of 50 r and the combined action of radiations and vibration (70 cps, 0.4 mm, exposure 15 min.) on the number of leukocytes in the peripheral blood of rats.

1 — control; 2 — radiated animals; 3 — animals exposed to a combined action. Crosses — average changes in these indices among animals exposed to these radiations during the fall-winter season (Livshits, Meyzerov, 1967).

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From Fig. 2 it can be seen that the first and second radiations caused no essential differences (according to this index) between control and test animals. After the third radiation the average relative strength of a conditioned reflex to Tone + nevertheless exceeded the initial level, but to a lesser degree than in the control group. The difference between the test and control increased a week after the third radiation. The relative strength of this reflex in radiated animals remained lower than in the controls during the entire period of later observations, but the difference was not statistically reliable.
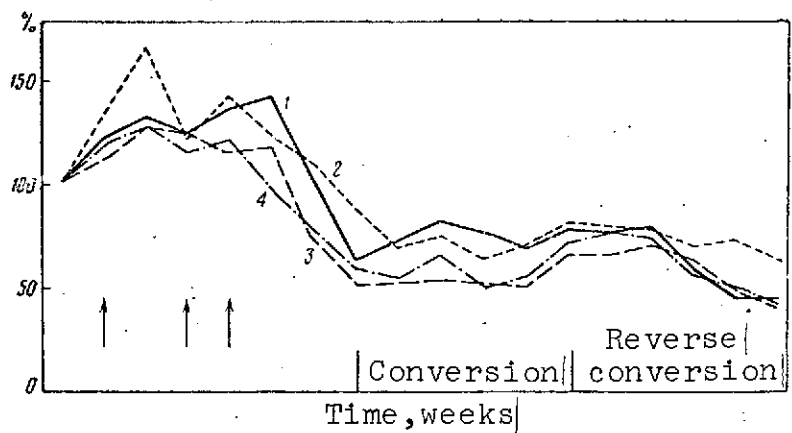
Figure 2. The effect of radiations, vibration and the combined action of
these factors on the average strength of a conditioned reflex to Tone +
in rats.

1 — control; 2 — animals exposed to vibration; 3 — animals exposed to radiations;
4 — animals exposed to combined forces; vertically — average test index (in %
of initial level, taken as 100%); arrows — forces.

Parameters of forces same as indicated in Fig. 1.
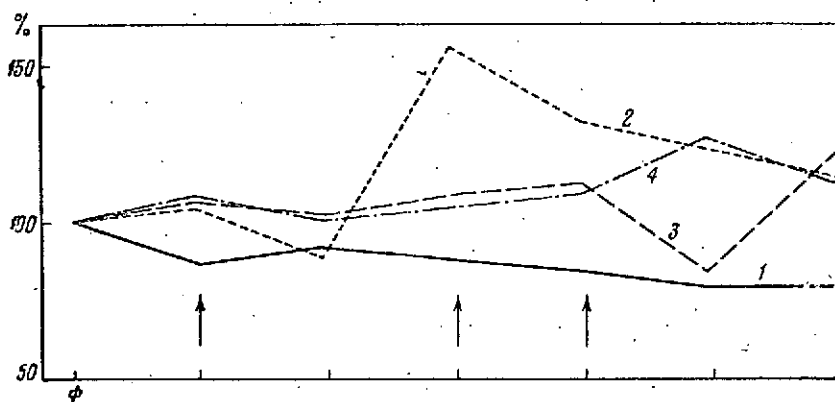


Figure 3. The effect of radiations, vibration and the combined force of these
factors on the average length of the latent period of a conditioned reflex
to Tone +.

Symbols same as in Fig. 2.

Development of a conditioned reflex to light was begun the day before the first radiation; therefore, we had no possibility of expressing its strength in percentages of the initial background. Visual comparison of absolute values of this parameter show that the difference between its average values in the control and radiated groups did not increase during the process of radiations. This indicates that we were not able to capture the action of radiation in this index.

The strength of conditioned reflexes to Tone + and Light in animals undergoing the combined force did not differ from that in the radiated group. Here not only were statistically reliable differences lacking, but also the curves representing the dynamics of changes in these indices in these groups were visually extremely close.

From Fig. 2 it can be seen that in animals exposed to vibration, after the first exposure the strength of the conditioned reflex on Tone + was greater than in the control and later the value of this parameter fluctuated about the level of the control, sometimes exceeding it, sometimes dropping below. At none of the steps of observation were differences statistically reliable.

Changes in the number of phase phenomena in each of the test groups did not exceed the fluctuations in frequency of such cases in the control.

A completely different picture was noted in comparing changes in the latent periods to Tone + in test groups. The average latent periods of this reflex, expressed in percentages of the initial background, in each of the test groups exceeded that in the control after the first force and these differences remained regular throughout the entire observation period (Fig. 3). The longer average length of the latent period in test groups in comparison with the control was statistically reliable (p<0.05).

No differences were detected between changes in this index in radiated animals and animals exposed to a combined force. Curves representing the dynamics of changes in the latent period to Tone + in these groups practically coincided. The separation between them at one point (after termination of the forces) is unreliable.

The latent period of the conditioned reflex to Light in all test groups was reliable longer than in the control. Unfortunately, in view of lack of

data on this index before application of the forces, it is impossible with confidence to assert that these differences were due to the forces and not to individual characteristics of the animals in different groups.

The strength of the reflex to Tone — in radiated animals was the same as in the control. In animals exposed to vibration and combined forces, the
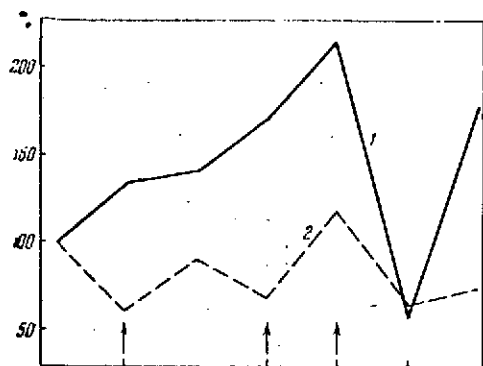
Figure 4. The effect of radiations on the average length of the latent period of reaction to Tone — (differentiation).

Symbols same as in Fig. 2.

strength of the reflex to differentiation was greater than in the control group, but the differences were not statistically reliable.

The relative value of the latent period of this reaction in all test groups was lower than in the control. In radiated animals (Fig. 4) and only in this group inhibition of differentiation was statistically reliable according to this index (p<0.05).

In three weeks after the third force, as in the work of Ye. M. Skobeyev, we began to convert signal values of the associated pair of stimuli (Tone + and Tone —) to the opposite values.

During the conversion, ratios between the parameters of both reactions in the control and test groups were maintained the same as before, i.e. no significant differences between compared groups were found during conversion.

Five weeks after the start of conversion we proceeded to reverse conversion of the signal value of this same pair of stimuli. In six weeks no complete reverse conversion in the strength of the conditioned reflex to Tone + was achieved in any of the test groups, which indicates the difficulty of this for our animals.

In rats exposed to vibration, the original latent period of the reflex to Tone + was restored more slowly than in control rats (p<0.01). The signal value of Tone — was converted more quickly than in the control (p<0.05). This indicates a change in the balance between stimulating and inhibiting processes.

In radiated animals changes were observed only during conversion of the reaction to Tone ⁻. Differences from the control were the same as in vibrated animals. In rats exposed to the combined forces, no reliable changes were noted during the course of conversion in any of the indices.

## Discussion of results

In these tests changes in conditioned reflex activity under the effect of all applied forces were significantly less pronounced than those described earlier [7]. The effect of radiations was also less significant in comparison with tests described in a later work [8]. This could be due to the considerable differences in the method of testing conditioned reflexes described above. It could be especially important that in both previous works tests were conducted daily and in the studies described here, as a rule, 3 times a week, making the task easier for the animals. But it remains unclear if methodological characteristics in this series of tests could explain the lack of differences between reactions of higher sections of the brain to radiations and combined forces, which in the previous work were statistically reliable. This question required further study.

Our tests reveal a significant difference between the effect of applied forces on conditioned reflex activity and on maze learning. In the works of Ye. M. Skobeyev [11-13] no statistically reliable deterioration was found in test groups in maze learning according to any indices. In our tests all forces we used caused a lengthening of the latent period of the conditioned reflex to Tone +.*  In addition, in radiated animals the latent period of the reaction to differentiation was reliably shorter than in the control. In control rats during the application of the forces this index lengthened under the influence of training. At the same time training had no effect on the latent period of the reaction to Tone ⁻ in rats exposed to radiation.

We can consider these phenomena as proof of our assumption that the conditioned reflex method better reveals disturbances of higher nervous activity caused by radiations, vibration and combined forces than studying the behavior of animals in a maze.

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*Here we do not consider the fact of the lengthened latent | period to light for the reasons indicated above.

We tried to do everything so that the methodological conditions of our experiments would be identical with those of Ye. M. Skobeyev which we described in detail above. However, for technical reasons we were not able to do this in one respect: Ye. M. Skobeyev exposed his animals to forces in small groups during the autumn, winter and early spring. We exposed all animals to the forces at the same time between Aug. 20 and Sept. 10.

In order to reveal the role which seasonal and meteorological factors /50 played in the general radiosusceptibility of our animals, we compared leuko-penic reaction of our rats with those of rats exposed to radiations in approximately the same seasons as the rats of Ye. M. Skobeyev. These data are given in Fig. 1. This figure shows that according to this index there is no basis for considering the population of rats we used as more radiosusceptible than those radiated during the fall-winter and spring seasons. In addition, we would also have to take into consideration the large variability of higher nervous activity of rats and their reactions to radiation and dynamic factors. For complete confidence in the results it would be desirable to compare the effect of these forces on conditioned reflexes and maze learning in tests conducted simultaneously on the same animals, which was done in the following work .

## Conclusions

1. Three forces of general vertical vibration with a frequency of 70 cps, amplitude of 0.4 mm, exposure of 15 minutes, three general x-ray radiations in single doses of 50 r and combined forces of these factors caused a reliable lengthening of the latent period of the conditioned reflex in rats.

2. The latent period of the reaction to differentiation stimulus in rats exposed to radiation was shorter than in control animals.

3. Analogous forces administered earlier to other groups of animals caused no reliable deterioration of maze learning.

## REFERENCES

1. Apanasenko, Z.I. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 92.

2.  Gol'dberg, M.B., I.A. Kolomiytseva, V.N. Semagin, A.Ye. Sharov and Ye.V. Sharova. Trudy Institute vysshey nervnoy deratel'nosti, Pathophysiology series. Vol. 10, 1962, p. 187.

3.  Lebedinskiy, A.V. and Z.N. Nakhil'nitskaya. Vliyaniye ioniziruyushchikh izlucheniy na nervnuyu sistemu (The Effect of Ionizing Radiations on the Nervous System). Moscow, Atomizdat., 1960.

4.  Livshits, N.N. Vliyaniye ioniziruyushchikh izlucheniy na funktsii tsentral'noy nervnoy sistemy (The Effect of Ionizing Radiations on Functions of the Central Nervous System). Moscow, Izd-vo AN SSSR, 1961.

5.  Livshits, N.N. Radiobiologiya, Vol. 7, No. 5, 1967, p. 790.

6.  Livshits, N.N., Z.I. Apanasenko, V.Ya. Klimovitskiy, A.P. Korolevskiy, M.A. Kuznetsova, L.D. Luk'yanova and Ye.S. Meyzerov. Uspekhi sovremennoy biologii, Vol. 67, No. 2, 1969, p. 256.

7.  Livshits, N.N. and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 236.

8.  Livshits, N.N., Ye.S. Meyzerov, R.M. Zakirova and V.A. Tikhaya. In the /51 book: "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 169.

9.  Luk'yanova, L.D. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 145.

10. Pavlov, I.P. Polnoye sobraniye sochineniy (Complete Collected Works) Moscow-Leningrad, Izd-vo AN SSSR, Vol. 3, Book 2, 1951, p. 175.

11. Skobeyev, Ye.M. Radiobiologiya, Vol. 10, No. 4, 1970, p. 619.

12. Skobeyev, Ye.M. Radiobiologiya, Vol. 10, No. 5, 1970, p. 715.

13. Skobeyev, Ye.M. This Collection, 1973, p. 121.

14. Furchtgott, E.J. Compar. Physiol., Vol. 44, 1971, p. 197.

15. Furchtgott, E.J. Psychol. Bull., Vol. 60, 1963, p. 157.

16. Levinson, B. Compar J. Physiol. Psychol., Vol. 45, No. 2, 1952, p. 140.

17. Stahl, W.R. J. Nerv. Ment. Dis., Vol. 126, 1959, p. 511.

# STUDY OF THE EFFECT OF VIBRATION,
## RADIATIONS AND A COMBINATION OF THESE FACTORS
## ON CONDITIONED REFLEXES AND MAZE LEARNING
### IN TESTS ON THE SAME ANIMALS

N. N. Livshits, Ye. S. Meyzerov,
R. M. Zakirova, V. A. Tikhaya

We showed that three applications of vibration (70 cps, 0.4 mm, 15 min.), radiations in single doses of 50 r and a combination of these factors caused a reliable deterioration in several indices of food conditioned reflexes in rats. Earlier Ye. M. Skobeyev found that these forces do not cause significant deterioration of maze learning developed to food reinforcement in rats (see our preceding article in this collection).

These data could be considered as proof of our assumption [2, 3] that the conditioned reflex method better shows disturbances in functions of higher sections of the central nervous system than study of the behavior of animals in a maze. However, such a conclusion could not be considered completely proven, as study of conditioned reflexes and maze learning was conducted at different times and on different groups of animals. The effect on the results of the variability of test reactions in different rat populations could not be excluded, nor could seasonal and meteorological factors. To eliminate these objections, in this work parallel studies of the effect of vibration, radiation and combined forces on conditioned reflex activity and maze learning were conducted with the same animals.

In addition, we were faced with the problem of proving our previous data on the influence of vibration on radiation effects. Earlier we found that second and third vibrations with subsequent radiation caused more significant /52 disturbances of conditioned reflex activity than each of these factors individually [4]. In a later work (see the article by these authors in this collection) this change could not be reproduced. It was advisable to test the possibility of increasing the influence of vibration on radiation effects with

still another modification of the technique.

## Technique

Conditioned reflex tests were conducted in the unit described in the preceding work and according to the same stereotype. Several changes were introduced into the experimental technique. Forces necessary to open a door blocking access to the feeding trough below certain amplitudes were measured in grams and the integrator indicator was calibrated according to these data.

Conditioned reflexes to Tone + and Light (270 and 170 associations, respectively) were developed and firmly fixed in the rats. Differentiation was exhibited 25 times and its development was not completed. At this stage conditioned reflex tests were temporarily interrupted and maze learning was begun in the rats.

A plan of the maze is given in Fig. 1. Three sunflower seeds placed in the feeding compartment served as reinforcement. The rat was placed in the start compartment. The experimenter raised the door blocking the exit to the
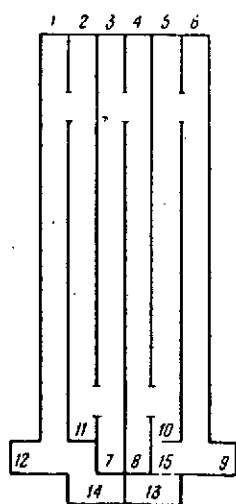


Figure 1. Diagram of the maze used in the tests described, as well as in the work of Ye. M. Skobeyev.

1-6 — paths; 7-12 — blind alleys; 13 — starting compartment; 14 — feeding compartment

maze. Time between exit of the rat from the start compartment and achievement of the goal was recorded automatically by means of an electronic millisecond timer. If the rat did not reach the goal in 5 minutes the test was considered unsuccessful. The floor of the maze was made of 50 platforms measuring 10 x 10 cm. Entry of the rat onto a platform not leading to the goal was considered an error. The number of errors was recorded visually by the experimenter. When any of the rats achieved the first criterion of "skill", i.e. one errorless

run through the maze, its tests were interrupted until the other rats reached this criterion. When the first criterion of "skill" has been attained by all rats (with the exception of three) we started to test conditioned reflexes /53 and maze learning the same day. Tests in which conditioned reflexes were tested immediately before maze learning were alternated with tests in which these methods were used in reverse order.

Experiments by both methods were conducted daily except holidays; 3 times a week food was withheld for 4 hours before the test and twice a week 18-20 hours. In these cases only milk and vegetables remained in the cages. Two weeks after the start of such tests the rats were separated into four groups:

1st control group (8 rats),

2nd group exposed to vibration (6 rats),

3rd group of 9 animals, exposed to x-ray doses of 100 r, dose rate of 10 r/min. Other conditions of radiation were the same as described in the preceding | article.

4th group of animals exposed to vibration and radiation in doses of 100 r (9 rats). Vibration parameters were the same as in the preceding | series of tests. Forces were produced once.

The vibrostand and x-ray chamber were in adjacent rooms; the laboratory in which the animals were examined was 1-1.2 km from this building. The rats were conveyed to the tests by machine. Results of tests with four- and | twenty-hour deprivation of food were analyzed separately.

For statistical analysis we used the algorithm for comparing two regression series [7] and in individual cases Student's criterion. As these criteria are parametric, test indices were expressed not in percentages of the original, but as differences between average values before the forces.

### Results of studies

After the forces none of the above changes were noted in the general state of the animals. Weight of the animals fluctuated 1-2% above the initial level; no essential difference between control and test groups was found. In this series of tests the amount of leukocytes in the blood and higher nervous activity were studied in the same rats. In order to avoid traumatization of the animals, blood was analyzed only twice. Results of analysis are given in Table 1.

Transporting the animals to the site where the forces were applied, being placed in unusual circumstances, and returning to the laboratory were influencing factors and changes in indices of higher nervous activity in the control group were apparent.
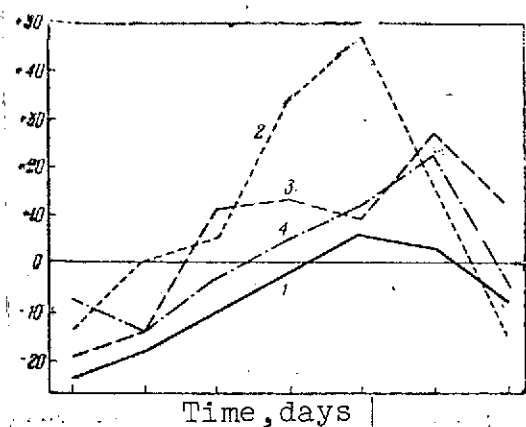


Figure 2. The effect of radiation in doses of 100 r, vibration and the combined force of these factors on average strength of conditioned reflex to Tone + in rats (food withheld for 4 hours before test).

Vertically — average test index, expressed as the difference from average initial background in arbitrary units. 1 — control; 2 — animals exposed to vibration; 3 — animals exposed to radiation; 4 — animals exposed to a combined force.

By both methods (conditioned reflex and maze) it was found that the effects of forces depend on the length of food deprivation. With 4-hour deprivation, changes in several indices of conditioned reflex activity indi-

Table 1

AVERAGE NUMBER OF LEUKOCYTES IN PERIPHERAL BLOOD IN CONTROL AND TEST GROUPS

| Force | Number of leukocytes in 1 mm$^3$ of blood | |
|-------|-------------|-------------------|
|       | before force | 2 days after force |
| Vibration | 18,500 | 15,583 |
| Radiation | 13,811 | 6,364 |
| Combination | 13,666 | 7,755 |
| Dummy (control) | 12,975 | 15,937 |

cated an increase in stimulating processes. The strength of the conditioned reflex to Tone + increased in all test groups (Fig. 2). Differences between the strength of this conditioned reflex in radiation and vibration groups and the control were reliable ($p < 0.05$ and $p < 0.01$ respectively). Under these con-
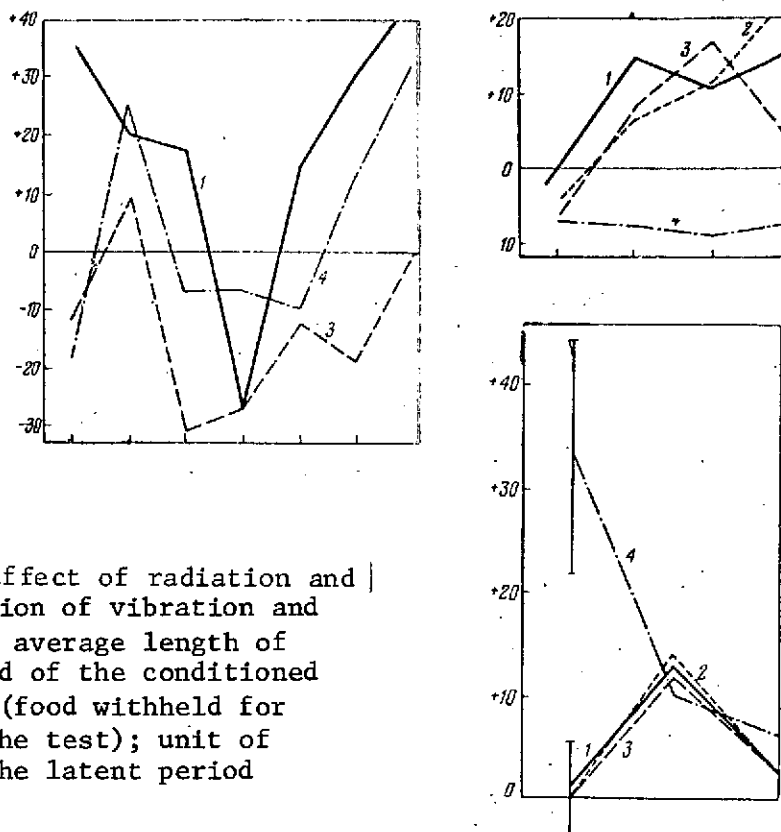
Figure 3. The effect of radiation and |
the combined action of vibration and
radiation on the average length of
the latent period of the conditioned
reflex to light (food withheld for
4 hours before the test); unit of
measurement of the latent period
0.1 sec.

Other symbols and parameters of
forces are the same as in Fig. 2.

Figure 4. The effect of radiation, vibration and the combined action of these|
factors on the average strength of the conditioned reflex to light (food
was withheld for 18-20 hours before the test.

Parameters of forces and symbols same as in Fig. 2.

Figure 5. The effect of radiation, vibration and the combined action of these |
factors on the average strength of the conditioned reflex to Tone — (dif-
ferentiation) (food was withheld for 18-20 hours before the test).

Parameters of forces and symbols same as in Fig. 2.

ditions deprivation in animals exposed to radiations and to combined forces

shortened the latent period of the conditioned reflex to Light (Fig. 3).

Differences from the control group were reliable (p<0.01 and p<0.05 respec-

tively). Indices of the reaction to differentiation in these groups did not

change significantly.

With 20-hour food deprivation no increase was observed in the strength
or no shortening of latent periods of conditioned reflexes in test groups.

In the group exposed to the combined force, the total length of time
during which the door was closed during the operation of Tone + changed.
This parameter, as is known, is the sum of two values: the latent period of
the conditioned reflex and the time of closing the door, i.e. cessation of
the conditioned reaction after the first push at the door.
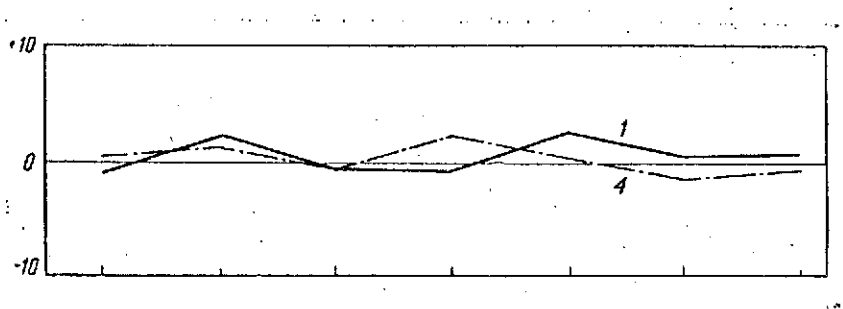
Figure 6. The effect of radiation, vibration and the combined action of these
factors on the number of errors in the maze (food withheld for 4 hours before
the test).

Parameters of forces and symbols same as in Fig. 2.
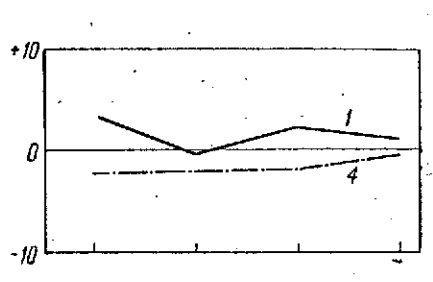


Figure 7. The effect of radiation,
vibration and the combined action
of these factors on the number of
errors in the maze (food withheld
for 18-20 hours before the test).

Parameters of forces and symbols
same as in Fig. 2.

Changes in this index were undulating. It increased on the 1st day of
observation, decreased on the second and increased again on the 4th day,
indicating instability of this reaction.

Differences from the control were reliable according to the criteria of
differences and nonparallelism of series [7], p<0.01. In these animals the
average strength of the conditioned reflex to light was reduced during the
entire period of observations (Fig. 4). Differences from the control were
reliable (p<0.05). The length of the latent period of this stimulus was in-

creased, but differences from the control were not reliable.

In this group on the 2-3rd day after the| force the strength of the re-action to differentiation of Tone — increased (Fig. 5). Differences from the control were reliable according to Student's criterion (p<0.05).

In tests run with 4-hour deprivation of food, in none of the test groups were reliable changes in time crossing the maze or the number of errors ob-served after application of the forces. From Fig. 6 it can be seen that fluctuations in the relative frequency of errors in the maze do not exceed the limits of those in the control group.

In tests conducted against a background of 18-20 hour deprivation of food, in animals exposed to the combined action, the number of errors in the maze decreased in comparison with the normal initial background and the con-   /57 trol (p<0.001, see Fig. 7). The time for crossing the maze decreased (p<0.05). A reduction in the number of errors in the maze under these food deprivation conditions was also noted in a group of rats subjected to vibration (p<0.05). In radiated animals no reliable changes| were recorded in this index.

For clarity data on parameters by which reliable differences between the control and test groups were detected are combined in Table 2.

Table 2

DIFFERENCES BETWEEN CONTROL AND TEST GROUPS ACCORDING TO THE INDEX OF HIGHER NERVOUS ACTIVITY

| Index of higher nervous activity | Length of food deprivation hours | Force | Statistical criterion | Direction of changes after forces | p |
|---|---|---|---|---|---|
| Strength of conditioned reflex to Tone — | 4 | Radiation (control) | Excess of one regression series over the others according to N. A. Plokhinskiy | Strength of conditioned reflex increased | <0.05 |
| | | Vibration (control) | Same | Same | <0.01 |

Table 2 (continued)

| Index of higher nervous activity | Length of food deprivation hours | Force | Statistical criterion | Direction of changes after forces | p |
|---|---|---|---|---|---|
| Latent period of conditioned reflex to Light | 4 | Radiation (control) | " " | Latent period shortened | <0.01 |
| | | Combined forces (control) | " " | Same | <0.05 |
| Number of errors in maze | 18-20 | Same | " " | Number of errors decreased | <0.001 |
| Number of errors in maze | 18-20 | Vibration (control) | Excess of one regression series over the others according to N. A. Plokhinskiy | Number of errors decreased | <0.001 |
| Time crossing the maze | 18-20 | Combined force (control) | Same | Time crossing the maze decreased | <0.05 |
| Strength of conditioned reflex to Light | 18-20 | Same | " " | After force strength of conditioned reflex reduced | <0.05 |
| Strength of conditioned reflex to Tone − | 18-20 | Same | Student's criterion | Inhibition of differentiation on second, third days after force | <0.05 |
| Time of closing door during operation of signal Tone + | 18-20 | Same | Criterion of algorithm according to N.A. Plokhinskiy | Two-phase reaction | <0.01 |

In this and previous works we used comparatively small doses of radiation whose action on higher nervous activity was extremely variable; therefore, we could not expect demonstrative effects. Such doses were selected so that it would be difficult to compare quantitative disturbances of conditioned reflex activity and maze learning. Therefore, we planned experiments so that changes could be expected in one of the test forms of higher nervous activity but not in the other, or evident qualitative differences of effects.

Two variants of the experiments were conducted.

1. A comparison of the action of test factors on conditioned reflex activity in some groups of animals and maze learning in other groups of animals under conditions as identical as possible.

2. Comparison of the effects of these factors on conditioned reflex activity and maze learning in tests on the same animals.

Each of these examples has inherent drawbacks. In the first of the described methods, it is difficult to create completely identical conditions as the interference of factors uncontrolled by the experimenter is always possible and an important role is played by the variability of radiosensitivity among animal populations.

The second method we used does not have this drawback, but testing conditioned reflexes and maze learning in the same animal places it in a difficult situation. Results can be different from those obtained by using only one method.

But we obtained basically the same data in both cases, which indicates they are reliable. In the first study in all test groups the conditioned reflex method revealed statistically reliable deterioration of one index of higher nervous activity (the latent period of the conditioned reflex to Tone +). In addition, in radiated animals inhibition of differentiation was observed. In the works of Ye. M. Skobeyev* it was not possible to find statistically reliable deterioration of any index of maze learning.

In this work indices of conditioned reflex activity in animals exposed to the forces reliably improved if the tests were conducted after 4-hour

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*See references to preceding article [11-13].

deprivation of food. In vibrated and radiated rats the strength of the conditioned reflex to Tone + increased. In rats exposed to radiation and a combined force the latent period of the conditioned reflex to Light was shortened. Differentiation was, therefore, preserved. Tests conducted against a background of 18-20 hour food deprivation revealed improvement was no longer observed in indices of conditioned reflex activity and its reliable deterioration was recorded according to individual parameters (reduction of the strength of the conditioned reflex to light, inhibition of differentiation in the group of rats exposed to a combined force). Such a reaction can be considered as two-phase. The change of phases was due not to the development of the process in time, as tests with various levels of deprivation were alternated, but to the dependence of susceptibility of higher sections of the central nervous system on the level of food excitability.

Maze learning in animals exposed to forces in tests after 4-hour food deprivation did not change essentially. In those cases when experiments were conducted against a background of 18-20 hour deprivation of food, a reliable improvement in both indices of maze learning was observed. Deterioration was not recorded in our tests in any parameters or in any of the groups of animals.

The phase of improvement of conditioned reflex activity and maze learning has been repeatedly described and discussed in the literature, beginning with works published by M. I. Nemenov in the 1930s and generalized in his monograph [5] and ending recently [9]. Assumptions have been made about the mechanism of these phenomena [1, 2, 3, 9]. We cannot consider this question here as it has no direct connection to the problems of this study. We only note that with perfectly identical forces we observed a phase of improved higher nervous activity in testing conditioned reflexes and maze learning but the phase of deterioration was detected only by the conditioned reflex method. This verifies our earlier assumption that the greater possibilities for revealing compensation of surgical damage of the cortex by studying the behavior of animals in a maze (indicated by I. P. Pavlov [6]), is also completely applicable to the action of radiation and dynamic factors. Maze learning can be considered as a chain conditioned reflex. In our maze, which has 7 points of choice, 7 differentiations should have been developed in the animals. Nevertheless, this learning was more reliable than the conditioned reflex stereotype with one

differentiation. The reliability is due to the fact that the animal in the maze utilizes signalization of various analysors and various effector systems for response. It is also very important that the rat in the maze uses information received through the kinesthetic analysor, which is the chief analysor for this kind of animal. In addition, the maze task corresponds to the ecology of the rat and it is possible that in the maze some natural conditioned reflexes are also realized. Our tests show that there are forms of higher /60 nervous activity with various degrees of reliability and, therefore, they are damaged in many different ways by the forces of dynamic and radiation factors.

In our tests we observed deterioration of individual indices of the conditioned reflex only in tests against a background of longer food deprivation. This contradicts the opinion of several radiobiologists who have assumed that changes in the characteristics of the conditioned reflex are determined by a reduction in the level of motivation in radiated animals [8, 9]. In fact, food excitability after radiation is reduced. But, if these authors were correct, a decrease in the conditioned reflex would sooner be expected after brief deprivation of food than after a longer period.

One of the purposes of our work, as stated above, was to prove that the radiation effect (which we described previously) is intensified as the result of preliminary vibrations. In a preceding study this effect was not verified, but in these tests reliable deterioration of several parameters of conditioned reflexes was recorded only in the group exposed to a combined force. Thus, we see here not very clearly, but, nevertheless, reliably facts revealing an increased radiation effect in cases of a combined force. This verifies the results of earlier published tests [4]. We also see that this effect is not always evident. It could be assumed that the lack of differences between the results of radiations and combined forces in the first series of tests could be caused by conducting conditioned reflex experiments every other day, which created a more favorable regime for higher nervous activity than daily tests.

The causes determining the results of a combined force on the functions of the central nervous system are discussed in more detail in the article of N. N. Livshits, Z. I. Apanasenko, V. Ya. Klimovitskiy, M. A. Kuznetsova, L. D. Luk'yanova and Ye. S. Meyzerov in this collection (p. 80).

## Conclusions

1. Three applications of general vertical vibration (70 cps, amplitude 0.4 mm, exposure 15 min.), general x-ray radiations in single doses of 50 r and combined forces of these factors caused a reliable lengthening of the latent period of the conditioned reflex in rats.

Analogous forces applied to other groups of animals did not cause reliable changes in maze learning.

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2. General x-ray radiation in doses of 100 r, vibration and a combined force increased the strength and shortened the latent period of several conditioned reflexes in rats in tests after 4-hour deprivation of food.

Against a background of 18-20 hour starvation, rats exposed to a combined force exhibited a reduced strength of the conditioned reflex to light and brief, but reliable inhibition of differentiation.

3. In these same rats, in tests conducted after 4-hour deprivation of food, no reliable changes were detected in indices of maze learning.

In tests conducted against a background of 18-20 hour deprivation of food, in a group of animals exposed to a combined force, a reliable reduction was recorded in the number of errors in the maze.

4. Conditioned reflexes are a more accurate indicator of the damaging action of our applied stress factors than maze learning. Maze learning is a good index for judging the presence of compensation processes.

5. The possibility of increasing radiation effects after vibration forces produced immediately before radiation is verified. However, this effect was not always reproduced and, evidently, depended on many factors.

## REFERENCES

1. Lebedinskiy, A.V. and Z.N. Nakhil'nitskaya. Vliyaniye ioniziruyushchikh izlucheniy na nervnuyu sistemu (The Effect of Ionizing Radiations on the Nervous System). Moscow, Atomizdat., 1960.

2. Livshits, N.N. Vliyaniye ioniziruyushchikh izlucheniy na funktsii tsentral'noy nervnoy sistemy (The Effect of Ionizing Radiations on Functions of the Central Nervous System). Moscow, Izd-vo AN SSSR, 1961.

3. Livshits, N.N. Radiobiologiya, Vol. 7, No. 5, 1967, pp. 790 - 800.

4. Livshits, N.N. and Ye.S. Meyzerov. In the collection: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 236.

5. Nemenov, M.I. Rentgenoterapiya cherez vozdeystviye na nervnuyu sistemu (Roentgenotherapy Through Influence on the Nervous System). Leningrad, Medgiz, 1950.

6. Pavlov, I.P. Polnoye sobraniye sochineniy (Complete Collected Works). Moscow-Leningrad, Izd-vo AN SSSR, Vol. 3, Book 2, 1951, p. 175.

7. Plokhinskiy, N.A. Biometriya (Biometry). Moscow, Moscow State University, 1970.

8. Furchtgott, E.J. Psychol. Bull., Vol. 60, 1963, p. 157.

9. Kimeldorf, J. and E.L. Hunt. Ionizing Radiation: Neural Function and Behavior. N.Y.-London, Academic Press, 1965.

# CHANGE IN OXIDIZING METABOLISM OF NERVE TISSUE
## IN CONNECTION WITH THE RADIOPROTECTIVE EFFECT
## OF GENERAL VERTICAL VIBRATION

L. D. Luk'yanova, L. M. Murashko

We showed earlier that the effect of the combined force of vibration and radiation against a background of postvibration inhibition is expressed as a moderation of the aftereffects of radiation injury. ‘Concurrent in vivo studies of oxidizing metabolism revealed significant parallelism between changes in the functional state of the animals and disturbance of respiration in brain tissue [1-2]. The purpose of this work was to test in direct experiments the direction of metabolic changes connected with the operation of the respiratory chain of nerve tissue which occur during the development of radiation sickness in animals under the influence of the combined force of vibration and radiation.

## Methods

The study was conducted on slices of the cerebral cortex (sensorimotor section)(CC) and the motor section of the subcortex (caudate nucleus) of white male rats.

To compare the results with earlier data (in vivo) the animals were exposed to 15-minute vertical vibration (70 cps; 0.4 mm). Immediately following vibration or 15 minutes after they were radiated with a dose of 600 r (RUP-1, 180 kv, Cu + Al). Selection of the interval of time between vibration and radiation was based on earlier data that the excitation phase accompanying vibration stimulation is replaced 10-15 minutes after vibration by postvibration inhibition [2, 3, 4]. Taking this into account, it has been assumed that radiation of animals immediately after vibration occurred against a background of generalized stimulation of the central nervous system (CNS), while that after 15 minutes took place during the period of maximum postvibration inhibition. On the next day after radiation the animals were exposed

to a second vibration similar to the first.

The brain was extirpated to obtain slices of nerve tissue: 1) an hour after radiation; 2) an hour after the second vibration (first day after radiation); 3) 3½ and 10 days after radiation.

Parallel with these tests and at the same time intervals an examination was made of other rats exposed to radiation alone. Vibration was replaced by listening to the noise of the vibrostand.

Serving as a control for all these tests were intact animals in which /63 the oxidizing metabolism in slices of the CC and caudate nucleus was also examined. The study was conducted on 175 rats. Seven animals were examined in each version of the tests.

Study of the respiratory metabolism of nerve tissue was conducted polarographically. Freshly-isolated slices were incubated in a glucose-salt medium. The reaction medium was Tyrode's solution (pH ± 7.4, t = 38°) without exogenous substrates of oxidation. During the measurements succinate and ADP were added. Reaction to this kind of addition made it possible to evaluate the functional state of nerve tissue by the pattern of metabolic responses.

## Results of the study

Figs. 1-4 (a) give curves of respiration for slices of brain from animals exposed to radiation at various times after vibration. If follows that under the influence of the test forces, in various sections of the cerebrum phase changes develop in the respiration of nerve tissue and its metabolic reactivity. Three periods are distinguished when characteristics of the tested metabolic processes change sharply: the 1st, 5th and 10th days.

The direction of changes and the degree of their severity vary in different brain structures. Very important is the time interval separating the vibration stimulus (or listening to it) and subsequent radiation. If it was 15 minutes, respiration of CC tissue under the influence of a combined force differed little from the level of oxygen consumption of these same slices from control animals (Fig. 1, a). There was a small increase in respiration in the first hour after the force. Other deviations from normal were statistically unreliable. In the motor section of the subcortex in these animals, a sharp intensification of respiration was observed in the first 24 hours and then its

subsequent normalization.

With radiation alone (15 minutes after listening to the noise of the vibrostand) a small but reliable reduction was registered in endogenous respiration in the CC in the first half hour and an increase after 24 hours, 5 and 10 days.

In subcortical sections there was an increase in the respiration of the brain tissue throughout the entire test period, most pronounced after 24 hours and after 10 days (Fig. 2, a). If the time interval between vibration and radiation was 2 minutes (Fig. 3, a), there was a sharp intensification of endogenous respiration of the slices. Despite its slight reduction by the 5-10th day, with a high degree of probability (p<0.01) it exceeded the level of respiration in control slices.
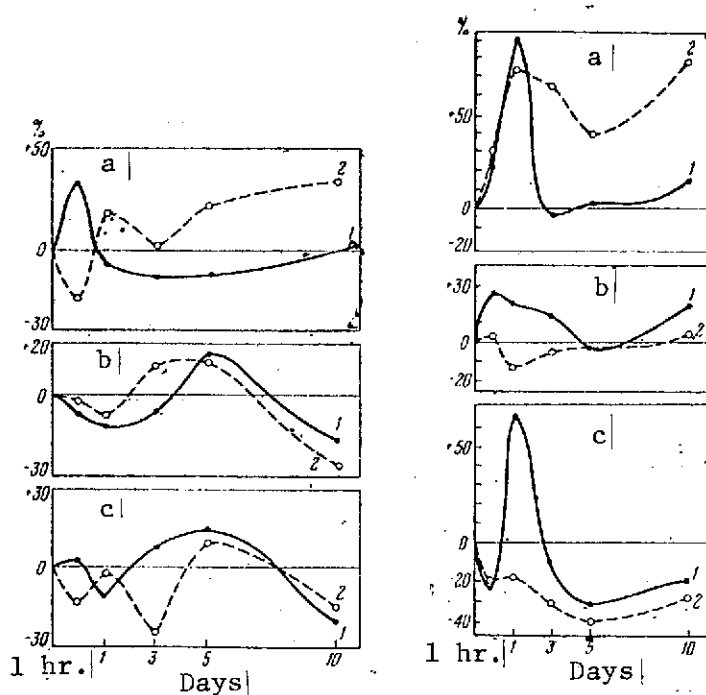
Figure 1.  Dynamics of changes in the respiratory activity of the CC in rats under the combined force of vibration and radiation with a 15-minute interval between them.

a — endogenous respiration of CC slices; b — respiration in the presence of succinic acid; c — respiration after the addition of ADP; 1 — animals exposed to the combined force; 2 — animals exposed to radiation alone.
Vertically — difference between test indices and those of intact animals.

Figure 2.  Dynamics of respiratory activity in the caudate nucleus of the CC of rats with the combined force of vibration and radiation with a 15-minute interval between them.  Symbols same as in Figure 1.

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In the motor section of the subcortex early changes (1-3rd day) were
analogous (Fig. 4, a). However, increase in the respiration rate progressed
for 10 days; this tendency was expressed most clearly in radiated animals.
Despite the fact that the criterion of reliability of differences between
radiation and a combined force in this case did not deny a null hypothesis
(p>0.05, although very slightly), the small reduction in the intensity of
respiration by the 5th day in the case of a combined force must not, evidently,
be considered accidental, as a reliable reduction in the same direction was
noted at this time in cortical sections of the brain.
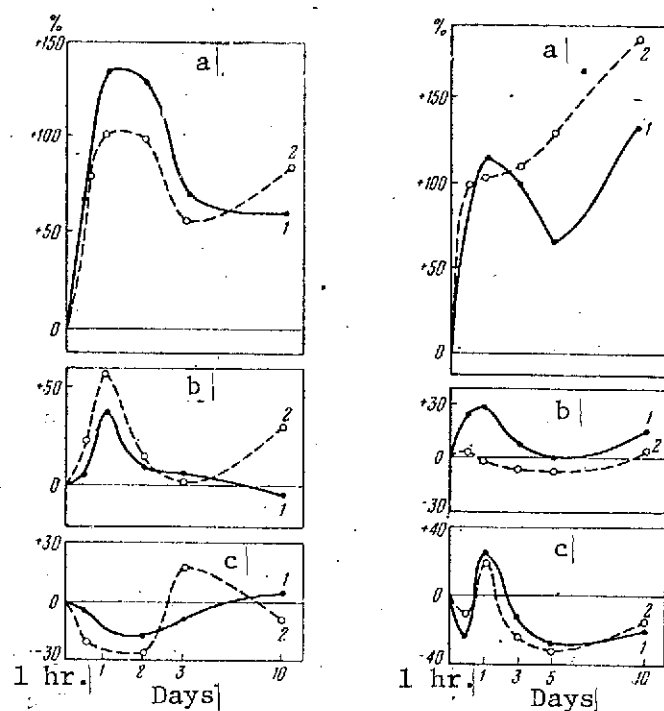
Figure 3. Dynamics of respiratory activity in the CC in case of a 2-minute
interval between vibration and radiation.
Symbols same as in Figure 1.

Figure 4. Dynamics of respiratory activity in the caudate nucleus of the cere-
brum of rats with a 2-minute interval between vibration and radiation.
Symbols same as in Figure 1.

The ambiguity of the manifestation of vibration and radiation on res-
piration in various sections of the brain is, therefore, evident. It then
also follows that changes in endogenous respiration in slices of brain and motor
sections of the subcortex are more clearly pronounced than in the sensorimotor

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section of the cortex. With regard to the role of vibration, when the animals were exposed to vibration against a background of postvibration inhibition (15-minute interval with a combined force) changes connected with radiation were moderated in all tested sections. With radiation against a background of postvibration stimulation this effect was not observed.

Study of the metabolic reactivity of brain tissue of animals exposed to radiation and a combined force suggested the kinetics connected with work of the respiratory chain of nerve tissue. With a 15-minute interval between radiation and vibration the metabolic response to succinate in the sensorimotor section of the cerebral cortex was unchanged in comparison with the control with sufficient reliability. In radiated animals on the 10th day after application of the force (see Fig. 3, b) the activating influence of succinate was reduced ($p < 0.01$). Changes connected with the oxidation of succinate developing in subcortical formations were unreliable both in radiated animals and those exposed to a combined force throughout the entire examination period (see Fig. 2, b). /66

With radiation 2 minutes after vibration in the overwhelming number of cases respiration increased in response to the addition of succinate in the first 24 hours. The degree of these changes was of the same order in the cortex and in the subcortex. A second reliable increase in the stimulating effect of succinate was observed in radiated animals in cortical sections on the 10th day. However, there were no changes in respiration in these animals in the subcortical area in general.

As a result of the action of these factors, therefore, changes connected with the oxidation of succinate in the cerebral cortex and motor area of the subcortex could in general not appear or be detected only briefly. They were more pronounced in the CC of animals radiated 2 minutes after vibration or after listening to the noise of the vibrostand.

The addition of ADP also altered the respiration of slices in the cerebral cortex and subcortex ambiguously. In cortical sections the action of ADP was similar in different versions of the tests and did not depend on the time interval. This was especially evident with radiation only of the animals when the character of reaction to ADP was reproduced in exactly the same direction in different sections of the brain (see Fig. 1, c; 3, c), differing only in the

degree of deviation from the control. It was expressed in an initial reduction of the stimulating effect of ADP and its subsequent normalization. Because extreme points in Fig. 3, c reliably differed from normal, the general course of changes in both cases, evidently, must be considered as a regular reaction to radiation. The same was found with a combined force, although the strength of the initial reduction in the action of ADP in this case was weaker.

The direction of changes in the action of ADP was also repeated for sub-cortical sections, regardless of the time interval between the forces (see Fig. 2, c; 4, c).

With a high degree of probability we can assert there is a reduction in the effectiveness of ADP in the first hour after radiation. Absolute values of this change were not sufficient to establish their reliable deviation from normal; however, the direction of this phenomenon was reproduced in all cases.

The next period appearing 24 hours after radiation was accompanied by a clearly increased reaction to ADP. Finally there appeared one more period of
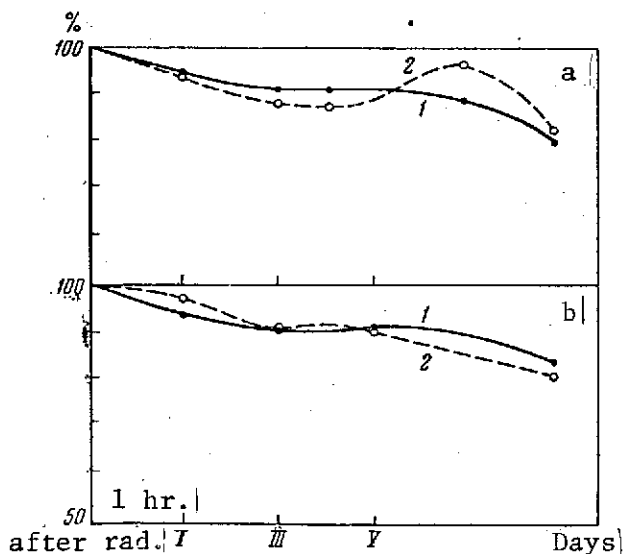
Figure 5. Change in the weight of animals after radiation (1) or a combined force (2) in case of 15 (a) and 2 minute (b) intervals between forces.

reduced ADP effectiveness, much more pronounced in both strength and duration. A different dynamic picture developed in radiated animals only (15 minutes after listening to the noise of the vibrostand) when no period of ADP activation was noted and the reduction (already in progress) of its regulatory role progressively increased up until the 5th day.

Clinical examination of rats showed that there are accurately determined differences in the lifetime of rats, changes in the blood picture, etc., when the animals are radiated against a background of postvibration stimulation or inhibition. Death of the animals in the second case occurs later than in the first. Also reliable are differences obtained in relation to the length of life with radiation and a combined force of vibration against a background of postvibration inhibition. They indicate a more acute course of radiation sickness in the first case.

We present average data (days):

| I (vibration 15 min. + radiation after 2 minutes) | II (vibration 15 min. + radiation after 15 minutes) | III (radiation 2 minutes after listening to the noise of vibrostand) | IV (radiation 15 min. after listening to the noise of the vibrostand) |
|---|---|---|---|
| 8.6±0.54 | 11.3 ± 0.60 | 11.7± 1.9 | 9.3 ± 0.52 |

Reliability of changes (by groups)

I-II ........ $p < 0.01$          II-IV ........ $p < 0.05$
I-III ........ $p > 0.05$          III-IV ........ $p > 0.05$

During the entire period of development of radiation sickness the animals    /68
lost weight. However, no reliable differences were found between radiated rats and those exposed to the combined force (Fig. 5)

Changes in the leukocyte formula of blood indicate the presence of the same acute and progressive form of leukopenia in animals exposed to separate radiation and in those radiated against a background of postvibration stimulation. At the same time, there were reliable differences in these indices with a 15-minute interval between vibration and radiation and with radiation alone. Beginning with the 5th day after radiation the drop in the number of leukocytes in the blood of animals exposed to a combined force lagged and by the 10th day the level of leukocytes in the blood reliably exceeded their amount in radiated animals. On the 10th day of radiation sickness, the number of leukocytes in the two last groups was 36±5 and 10±6% of normal, respectively.

## Discussion of results

Comparison of data obtained in the work verifies the assumption that the effect of radiation, realized against a background of postvibration intensification or inhibition of oxidizing metabolism in brain tissues is not ambiguous.

Despite the possibility of reproducing phase conditions in direct vibration stimulation of isolated nerve tissue (which we have indicated) in the integral organism the main focus of propagation of the pathological process is, evidently, the central nervous system. Of a different sort are forces lowering the excitability of cortical analysors or inhibiting their acceptance of proprioceptive impulses; they prevent the development of post-vibration inhibition, which we feel is excessive [5]. When an inhibited state is realized it appears in all other systems of the organism. According to our data, a sharp drop in oxidizing processes can be observed 20-30 min. after vibration in the lungs, liver and muscles. Therefore, a radiation force, following vibration, is realized against a background of general uniform functional adjustment of the entire organism.

This work verifies the conclusions| of earlier research conducted on animals in vivo that initial changes in oxidizing metabolism in the CNS, resulting from a vibration stimulus, affect and to a significant degree determine the development and course of radiation sickness.

With radiation against a background of postvibration activation of oxidizing metabolism in brain tissue, the development of radiation sickness and attendant symptoms are aggravated, while radiation during the period of inhibition of the work of the respiratory chain has a slight relieving effect on the course of development of the sickness.                    /69

Dynamic differences between groups of animals exposed to the combined force of vibration and radiation, as well as radiation with preliminary listening to the noise of the vibrostand in each of two test series, differing in the time interval between the forces, have a quantitative character and cannot always be considered reliable. The dynamic differences between the two series of tests are qualitative, as they are often determined by changes which are opposite in value and direction.

The metabolic reactions in different variants of the tests (the introduction of succinate and ADP) indicate the existence of definite deviations from normal in the oxidizing metabolism of nerve tissue, developing simultaneously with a number of functional changes in the central nervous system.

Three periods are distinguished in the development of these changes although in different sections of the brain they are accompanied by ambiguous changes in metabolic states.

In the first period (1st 24 hours) in the cerebral cortex of radiated animals as well as animals radiated against a background of postvibration stimulation (interval of 2 min.), endogenous respiration is intensified; succinate in the majority of cases has a stimulating effect; ADP inhibits respiration. By the degree of changes all series of animals could be arranged in the following order: combined force (interval of 2 min.)>radiation (2 min. after listening to the noise of the vibrostand)>radiation (15 min. after listening to the noise of the vibrostand).

In contrast, with the application of radiation against a background of postvibration inhibition (interval of 15 min.) endogenous respiration remains close to normal, but succinate has an inhibiting effect on the respiration of brain tissue.

In the second period (5th day) endogenous respiration of slices of the cerebral cortex remains high in animals in the first three series; succinate either has no effect on respiration or stimulates it; ADP stimulates respiration.

With radiation against a background of postvibration inhibition (interval of 15 min.) endogenous respiration changes little while the effect of succinate and ADP on respiration of slices is stimulating.

In the third period (10th day) endogenous respiration of slices of the cerebral cortex from animals in the first three series remains high as usual. Succinate stimulates respiration only in animals radiated 2 minutes after listening to vibration. In other cases it either has no effect or inhibits respiration. The inhibiting effect of ADP on respiration is predominant. In the group of animals radiated against a background of postvibration inhibition endogeneous respiration is close to normal but succinate and ADP reduce the intensity of oxygen consumption. This all indicates phase disturbances in

the mechanisms regulating oxidizing processes in nerve tissue.

Based on the assumptions stated in our other article in this collection concerning the possible effect of succinate on respiration in freshly isolated nerve tissue, it is obvious to assume that the most pronounced deviations from normal occur in the case of a combined force when radiation is conducted against a background of postvibration stimulation. They can indicate extreme activation of oxidizing processes in tissue, reaching maximum by the 5th day. From this information it follows that disturbances from a combined force are least severe when radiation is conducted against a background of postvibration inhibition. However, in this case there is also a critical period — the 5th day. Changes in tissue respiration in the cerebral cortex at this time are in the same direction as those in other groups of animals. We recall that according to our other data [3], 5 days is the breaking point in the development of radiation sickness, followed either by death of the animal or its recovery.

In the subcortical sections of the brain three periods are also distinguished when metabolic forces can cause variously-directed effects. Unlike the cortex of the brain, the most pronounced deviations from normal were observed here in the first 24 hours. The regularity of distribution of the degree of changes in different series of tests noted for the cerebral cortex is reproduced: combined force (radiation against a background of postvibration stimulation)>radiation (2 min. after listening to the noise of the vibrostand)> >radiation (15 min. after listening to the noise of the vibrostand)>combined force (radiation against a background of postvibration inhibition).

Phase changes in oxidizing metabolism in different sections of the brain resulting from radiation and a combined force, therefore, develop not only in the same time intervals as other physiological indices characterizing the severity of radiation injury, but they coincide with and, evidently, reflect known functional disturbances revealed in the central nervous system (specificity of changes in the cerebral cortex and subcortical sections) [8].

It is especially necessary to dwell on the role of the noise component. The existence of reliable differences in the oxidizing metabolism of radiated animals with subsequent (after 2 and 15 min.) listening to the noise of the vibrostand indicated the undoubted effect of this factor on the course of

radiation sickness.

The noise component is, evidently, far from indifferent from the point of view of the formation of a general functional background. Earlier it was shown that listening to the noise of the vibrostand (120 db) causes definite changes /71 in the oxidizing metabolism of the central nervous system and in conditioned reflex activity of the animals. However, the action of this stimulus faded after several applications [6-7]. In this work the noise component was also evidently an active factor. A more detailed study of this question would be of undoubted interest.

Experimental material indicates that there are several differences in the length of life of animals in comparison with data from our earlier works where the protective effect of postvibration inhibition was weaker. Comparison of the characteristics relating to the level of oxidizing metabolism of the brain of control animals used in both cases indicates seasonal influences. In the first case, all experiments were conducted in winter (December-March) with the average air temperature in the rooms 19-21°. In the second, they were during the summer (July-August) with the average air temperature 25-26°. The effect of the temperature factor, increasing metabolic processes and thereby reducing the effectiveness of artificial protection, is completely probable.

Nevertheless, the basic tendency established earlier is verified in this work. A more favorable course of radiation sickness occurs when animals are radiated against a background of vibration inhibition. These tests become even more persuasive in the light of data obtained in the work concerning intensification of the effect of radiation when it is realized during the period of postvibration stimulation.

REFERENCES

1. Livshits, N.N. and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 68.

2. Luk'yanova, L.D. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 60.

3.   Luk'yanova, L.D.   In the book:   "Vliyaniye ioniziruyushchikh izlucheniy
     i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy"
     (The Effect of Ionizing Radiations and Dynamic Factors on Functions of
     the Central Nervous System).   Moscow, "Nauka", 1964, p. 145.

4.   Luk'yanova, L.D., A.V. Kol'tsova, Ye.S. Meyzerov and Ye.P. Kazanskaya.
     In the book:   "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsen-
     tral'noy sistemy" (The Effect of Space Flight Factors on Functions of
     the Central Nervous System).   Moscow, "Nauka", 1960, p. 105.

5.   Luk'yanova, L.D. and S.M. Ambrosova.   In the book:   "Vliyaniye faktorov
     kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The
     Effect of Space Flight Factors on Functions of the Central Nervous
     System).   Moscow, "Nauka", 1966, p. 95.

6.   Luk'yanova, L.D. and Ye.Ts. Kazanskaya.   In the book:   "Vliyaniye faktorov
     kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The
     Effect of Space Flight Factors on Functions of the Central Nervous
     System).   Moscow, "Nauka", 1966, p. 81.

7.   Luk'yanova, L.D. and Ye.P. Kazanskaya.   Fiziol. zhurn. SSSR., No. 53, 1967,
     p. 563.

8.   Livanov, M.N.   Nekotorye problemy deystviya ioniziruyushchey radiatsii na
     nervnuyu sistemu (Some Problems of the Effect of Ionizing Radiation on
     the Nervous System).   Moscow, Medgiz, 1962.

# BASIC REGULARITIES IN THE COMBINED EFFECT
## OF DYNAMIC FACTORS AND RADIATIONS
## ON FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM

N. N. Livshits, Z. I. Apanasenko. V. Ya. Klimovitskiy,
M. A. Kuznetsova, L. D. Luk'yanova, Ye. S. Meyzerov

The studies of the combined effect of ionizing radiations and dynamic factors on functions of the central nervous system (CNS) presented in this collection are a continuation and to a certain extent the completion of a series of studies published earlier by this group of authors. The purpose of this article is to systematize and generalize all existing material and reveal general regularities and possible mechanisms of the combined action of stress factors.

## Material and methods

We studied the separate and combined effect of dynamic factors (vibration and accelerations) and ionizing radiation on electromyographic reactions of extensors of the hind limb with adequate stimulation of the vestibular analysor, unconditioned motor defense reactions to electric skin stimulation, conditioned motor food reflexes and oxidizing metabolism in brain tissues.

The methods of study used have been described in the articles of Z. I. Apanasenko, M. A. Kuznetsova, N. N. Livshits et al., L. D. Luk'yanova and L. M. Murashko, published in this collection.

Information on parameters of these forces, test indices and test animals is contained in Table 1.

## RESULTS

### 1. Types of reactions to combined forces

Despite the diverse conditions of the force, in the majority of cases the results were essentially alike.

Reactions to a combined force were of five basic types (indicated in the first article in this collection).

Table 1

PARAMETERS OF APPLIED FORCES, FUNCTIONS OF THE CENTRAL NERVOUS SYSTEM
STUDIED AND TEST ANIMALS

| Series | Force | CNS functions studied | Object of study | Author |
|---|---|---|---|---|
| I | General gamma radiation ($Co^{60}$). Dosage 500 r, dose rate 261 r/min. 50 min. before and 24 hours after radiation, general vertical vibration (70 cps, amplitude 0.4 mm, 15 min.) | Bioelectric activity of extensors of hind limbs in a state of relative quiet. Basic characteristics of vestibulomuscular reflex | Male guinea pigs weighing 350–500 g | A. I. Apanasenko [2] |
| II | Same | Threshold of excitability and latent period of motor defense reaction | Same | M. A. Kuznetsova [20] |
| III | General x-ray radiation 600 r (RUP-1 unit, filters: copper 0.5 mm, aluminum 0.75 mm, dose rate 22–43 r/min.) . 15 minutes before and 24 hours after radiation, vibration | $O_2$ pressure in brain tissues and rate of utilization of $O_2$ by tissues of the auditory and sensorimotor cortex and caudate nucleus | Male "Wistar" rats weighing 150–200 g | L. D. Luk'yanova [27] |
| IV | Same | Metabolic reactions of slices of cortex and caudate nucleus from animals killed at various times after application of forces | See III | L. D. Luk'yanova, L. M. Murashko* |
| V | First vibration 5 minutes before radiation. For other parameters see IV | See IV | See III | L. D. Luk'yanova, L. M. Murashko* |

Table 1 continued

| Series | Force | CNS functions studied | Object of study | Author |
|---|---|---|---|---|
| VI | General gamma-radiation (Co$^{60}$). Dosage 500 r, dose rate 0.6 r/min. Vibration 20-30 min. before and 2-2½ hours after radiation | See I. | Male guinea pigs weighing 350-500 g | Z. I. Apanasenko [3] |
| VII | General radiation. Dosage 100 r. RUP-200 unit, 190 kv, dose rate 30 r/min. Other conditions of radiation same as in III. Vibration 3-5 min. before radiation | Strength and latent periods of motor food conditioned reflexes | Male "Wistar" rats weighing 320-400 g during application of force | N. N. Livshits et al. |
| VIII | General gamma radiation (Co$^{60}$) five times. Single dose 100 r, dose rate 52 r/min. Intervals between radiations 3-4 days. Vibration 30-40 min. before and 24 hours after each radiation | See II | Male guinea pigs weighing 350-500 g | M. A. Kuznetsova [21] |
| IX | General x-ray radiation 3 times. Dose 50 r (RUP-11 unit , 200 kv, dose rate 33.3 r/min). For other conditions see III. Interval between first and second radiation 14 days, between second and third, 7 days. Vibration 3-5 min. before each radiation | See VII | Male "Wistar" rats. Age 14 months during application of forces | N. N. Livshits, Ye. C. Meyzerov [26] |

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Table 1 continued

| Series | Force | CNS functions studied | Object of study | Author |
|--------|-------|----------------------|-----------------|--------|
| X | Three radiations in the same dosage. For conditions see III. 3-5 min. before radiation, acceleration $-10g_{xe}$ 8 min. | See VII | Male "Wistar" rats. Weight during application of forces 400-450 g | N.N. Livshits et al., [25] |
| XI | General gamma radiation (cobalt-60), dosage 500 r, dose rate 200 r/min. 3 days before radiation, acceleration $-8g_x$ 15 min. | See I | Male guinea pigs weighing 350-500 g | Z. I. Apanasenko [4] |
| XII | General gamma radiation (cobalt-60). Dosage 500 r, dose rate 168 r/min. 7 days before radiation, acceleration $-8g_x$, 15 min. | See I | Male guinea pigs weighing 270-400 g | Z. I. Apanasenko* |
| XIII | Radiations same as in XI. 7 days before radiation, acceleration $-10g_x$, 4 min. | See I | See XII | Z. I. Apanasenko* |
| XIV | Radiation same as in II. 20 days before radiation the combined force of acceleration $-8g_x$ and angular velocity $70^0$/sec | See II | Male guinea pigs weighing 350-450 g | M. A. Kuznetsova** |
| XV | Acceleration $+6.3g_z$ 30-180 sec. | Blood flow, temperature of the brain and arterial blood | Rabbits Dogs | V. Ya. Klimovitskiy [11] |

Table 1 continued

| Series | Force | CNS functions studied | Object of study | Author |
|--------|-------|----------------------|-----------------|--------|
| XVI | Acceleration −5.4 $g_x$, 30–180 sec. | Temperature of the brain, arterial blood | Rabbits Dogs Rats | V. Ya. Klimovitskiy [12] |
| XVII | Hypoxia 5–10% $O_2$ 30–180 sec. | Blood flow, temperature of the brain and arterial blood | Rats Rabbits | V. Ya. Klimovitskiy** |

Note. 1. Vibration with the same parameters was used in all tests, therefore, they are indicated only in series I.
2. We used the following symbols to indicate the direction of accelerations: head–pelvis — +$ng_z$; back–chest — ¬$ng_x$; n — value of acceleration.

*Published in this collection.
**Data published for the first time.

1st type of reaction: domination in a combined force of the effect of the dynamic factor|throughout the entire period of observations, completely masking the effect of radiation.

An example of this type of reaction is change in the integral electric activity of extensor muscles of the hind limb of guinea pigs during the aftereffect of stimulation of the vestibular analysor. The animals were exposed to general radiation ($Co^{60}$) in a dose of 500 r and vibration twice (see Table 1, series I). /75

In radiated animals electric activity of the muscles undulated. Differences from the control group were statistically reliable according to the criterion of median ($p<0.01$) and dispersion ($p<0.05$). Vibration caused no reliable changes in this index. In the group exposed to a combined force there were also no reliable differences from the control animals or from animals exposed only to vibration. The radiation effect was completely masked by that of vibration.

2nd type of reaction: domination soon after radiation of the effect of the dynamic factor and later either predominance of the radiation effect or a complex combination of the effects of both factors. An example of this type

of reaction is discussed in the article by Z. I. Apanasenko in this collection (see Fig. 1, 2 in the second article).

Here we must also consider a variant of this type (type 2a): inter-| mediate position of the effect of a combined force soon after radiation and the domination of the radiation effect later. Z. I. Apanasenko described it in both articles (see Fig. 4, p. 22 and Fig. 7, p. 39).

The introductory article also discusses another variant of this type of reaction which is theoretically important: domination soon after the force of the effect of the dynamic factor and later the complex interaction of both agents. The effects of combined forces are intensified when they are weak and weakened when they are strong. An example of this variant is cited in the first article of Z. I. Apanasenko in this collection (see Fig. 6, p. 24).

3rd type of reaction: the intermediate position of the effect of a combined force between those of each factor independently during the main observation period.

This reaction was also observed in those cases when (in separate application) dynamic and radiation factors caused unidirectional effects but their action was opposite.

The latter case was described in the first article of Z. I. Apanasenko (in this collection)(see Fig. 5).

4th type of reaction: domination in some of the animals exposed to a combined force of the effect of the dynamic factor and in others that of the radiation factor or a combination of effects of both factors.

A description of this type was given in the same article by Z. I. Apanasenko (Fig. 7, p. 25).

5th type of reaction: mutual increase of effects of component factors. /78 This type of reaction is encountered relatively rarely (as yet it has been recorded only 5 times).

This type of reaction is discussed in the articles of N. N. Livshits, Ye. S. Meyzerov et al. (see Fig. 4, p. 55). A general summary of all experimental material is given in Table 2.

Table 2

TYPES OF REACTIONS TO A COMBINED FORCE

| Type of reaction | Series | Force | Index | Test index |
|---|---|---|---|---|
| 1. Domination of the dynamic factor throughout the entire observation period | VI | Prolonged radiation 500 r and vibration twice | 1 | Spontaneous bioelectric activity of extensor muscles of the hind limb |
| | XI | Radiation 500 r. 3 days before radiation, acceleration $-8g_x$, 15 min. | 2 | Bioelectric activity of the same muscles during adequate stimulation of the vestibular analysor |
| | XIII | Radiation 500 r. 7 days before radiation, acceleration $-10g_x$, 4 min. | 3 | Same |
| | XIII | Same | 4 | Bioelectric activity of these muscles in after-action of adequate stimulation of the vestibular analysor |
| | I | Radiation 500 r and vibration twice | 5 | Same |
| | IX | Radiation 50 r. 3-5 min. before radiation vibration. | 6 | Motor food conditioned reflexes |
| | X | Radiation 50 r three times. 5 min. before each radiation, acceleration $-10g_x$, 8 min. | 7 | Same |
| 2. Domination of the effect of the dynamic factor soon after the force and that of radiation or a combination of both factors later | I | Radiation 500 r and vibration twice | 1 | Spontaneous bioelectric activity of extensor muscles of hind limbs |
| | XI | Radiation 500 r. For 3 days before radiation, acceleration $-8g_x$, 15 min. | 2 | Same |

Table 2 continued

| Type of reaction | Series | Force | Index | Test index |
|---|---|---|---|---|
| | XIII | Radiation 500 r. For 7 days before radiation, acceleration —10 $g_x$, 4 min. | 3 | Same |
| | VI | Prolonged radiation 500 r and vibration twice | 4 | Bioelectric activity of these muscles during adequate stimulation of the vestibular analysor |
| | VI | Same | 5 | Same index in afteraction of adequate stimulation of the vestibular analysor |
| | XIII | Radiation 500 r; for 7 days before radiation, acceleration —10$g_x$, 4 min. | 6 | Latent period of electromyographic reaction to stimulation of the vestibular analysor |
| | I | Radiation 500 r and vibration twice | 7 | Length of aftereffect of stimulation of the vestibular analysor /77 |
| | VIII | Radiation five times in single doses of 200 r and vibration ten times | 8 | Latent period of unconditioned motor defense reaction |
| | III | Radiation 600 r and vibration twice | 9 | Pressure and rate of utilization of oxygen by tissues in different sections of the brain |
| 2a. Intermediate position of the effect of the combined force between the effects of each factor individually first and later domination of the radiation effect | XII | Radiation 500 r. For 7 days before radiation, acceleration —8$g_x$, 15 min. | 1 | Bioelectric activity of extensors of hind limbs with stimulation of the vestibular analysor |
| | XIII | Radiation 500 r; for 7 days before radiation, acceleration —10$g_x$, 4 min. | 2 | Length of aftereffect of stimulation of the vestibular analysor |

Table 2 continued

| Type of reaction | Series | Force | Index | Test index |
|---|---|---|---|---|
| 3. Intermediate position of the effect of a combined force between effects of each factor individually | I | Radiation 500 r and vibration twice | 1 | Bioelectric activity of extensor muscles of the hind limb with stimulation of the vestibular analysor |
| | I | Same | 2 | Latent period of electromyographic reaction to stimulation of the vestibular analysor |
| 3a. | VI | Prolonged radiation 500 r and vibration twice | 3 | Length of aftereffect of stimulation of the vestibular analysor |
| | XII | Radiation 500 r. For 7 days before radiation, acceleration $-8g_x$, 15 min. | 4 | Same |
| 4. Domination in some of the animals of the effect of the dynamic factor and in the others the radiation effect or a combination of the effects of both factors | XI | Radiation 500 r. For 3 days before radiation, acceleration $-8g_x$, 15 min. | 1 | Latent period of electromyographic reaction to stimulation of the vestibular analysor |
| | XII | Radiation 500 r. For 7 days before radiation, acceleration $-8g_x$, 15 min. | 2 | Same |
| | VI | Prolonged radiation 500 r and vibration twice | 3 | Same |
| | II | Acute radiation 500 r and vibration twice | 4 | Latent period of unconditioned motor defense reaction |
| | XIV | Radiation 500 r. For 20 days before radiation, acceleration $-8g_x$, 4 min. and angular speed 70°/sec. | 5 | Latent period of unconditioned motor defense reaction |

Table 2 continued

| Type of reaction | Series | Force | Index | Text index |
|---|---|---|---|---|
| | XII | Radiation 500 r. For 7 days before radiation, acceleration $-8g_x$, 15 min. | 6 | Bioelectric activity of extensor muscles of hind limb in after-action of stimulation of the vestibular analysor /78 |
| | XII | Radiation 500 r. For 7 days before radiation, acceleration $-8g_x$, 15 min. | 7 | Spontaneous bioelectric activity of extensor muscles of hind limb |
| | XI | Radiation 500 r. For 3 days before radiation, acceleration $-8g_x$, 15 min. | 8 | Length of after-effect of stimulation of the vestibular analysor |
| 5. Summation of effects of the dynamic and radiation factors during the entire period of observations | XI | Radiation 500 r. For 3 days before radiation, acceleration $-8g_x$, 15 min. | 1 | Bioelectric activity of extensors of hind limbs in after-action of of stimulation of the vestibular analysor |
| | IX | Three radiations in single doses of 50 r and vibration | 2-3 | Strength of motor food conditioned reflex to sound and light signals |
| | VII | Radiation 100 r and vibration | 4 | Strength of motor food conditioned reflex to weak stimulus (light) |
| | VII | Same | 5 | Strength of motor food reaction to differentiation |

Note. Numbers of series in this table correspond to those in Table 1, where parameters of forces are indicated in detail.

## 2. Conditions affecting the type of reaction

The domination of the influence of one of the component factors in a combined force depends on the strength of its individual effect on a given index. This is verified by the following experimental data.

1. Domination of the effect of radiation was usually observed later after the force at the height of radiation sickness when the action of radiation was most pronounced and that of the dynamic factor decreased.

2. Type 2a reactions, in which the influence of the dynamic factor on the effect of a combined force was least significant, were noted only in tests in which radiation was conducted 7 days after centrifuging, i.e. when its effect could already be weakened.

3. In reactions of type 4, a relation is noted between the individual response of the animal to a combined force and to acceleration alone. This could be traced in four cases when radiation was produced 3-7 days after the dynamic factors. The effect of acceleration dominated in those animals in which this index was changed most sharply under the influence of acceleration alone (See Fig. 6, p. 24).

Earlier we noted the similarity between cases of mutual increase of weak effects and weakening of strong effects of the separate action of combined factors and phase phenomena in the central nervous system [23]. If this similarity is not merely superficial, these facts also verify the theory that the effectiveness of each of the applied agents individually is important in the reaction to a combined force.

It can be assumed that dynamic and radiation factors create functional changes in structures of the CNS leading to paradoxical relations between the strength of the forces and the reaction. But the strength of the force on the function being tested is not the only factor determining the dominance of one factor in a combined force. Also playing a role here are the characteristics of the effective agent, so that sometimes the weaker effect can predominate.

We must note that a quantitative comparison of effects is not always possible. Different indices have different resistance to external forces and evaluation of the strength of a force by the shifts it causes is valid only within the limits of one index. It is also difficult to compare the effect

of dynamic and radiation factors by their values when they have opposite effects. Therefore, we introduced only two gradations of effectiveness of the force: weak and strong. We considered strong those forces which cause statistically reliable changes in the test index and weak those with no such effect. We considered lack of any marked difference later after the force between the studied index in test and control animals as a weakening of the effect at those times.

One example of the predominance of a weaker effect is the above-discussed 1st type of reaction in changes in the integral bioelectric activity of extensor /80 muscles of guinea pigs exposed to general gamma radiation and vibration twice. As stated in discussing this type of reaction, radiation caused reliable shifts in the test index, but in animals exposed to vibration no reliable difference from the control group was noted. Nevertheless, with a combined force the vibration effect completely dominated.

We give data on the domination (in a combined force) of the weaker effect of one of the combined factors (number of cases):

|  | Throughout entire period of observations | In several periods |
|---|---|---|
| Acceleration | -- | 7 |
| Vibration | 1 | -- |
| Radiation | -- | 1 |

Domination of the effect of the weaker factor was recorded in 9 cases; in 8 of these cases the weaker effect of the dynamic factor dominated and in only one, the radiation effect. The difference between dynamic and radiation factors in these reactions is reliable according to the criterion of signs ($p < 0.02$). With minimum effectiveness of the force on a given reaction, therefore, the influence of the dynamic factor in a combined effect dominates reliably more often than that of radiation. The greater effectiveness of dynamic factors on tested functions is also indicated by the fact that not once did we observe the domination of the effect of radiation in all animals during the entire period of observations. For vibration and acceleration such a reaction was noted in 7 cases, although in 6 of these the reaction to radiation in these

tests was very pronounced (see Table 3).

Thus, dynamic factors can sometimes also dominate in those reactions where their effectiveness is weaker than that of radiation. The number of such cases is rather high, so they cannot be considered exceptions. Therefore, it can be expected that the type of reaction of the central nervous system to a combined force according to any functional index will depend on the effectiveness of each of the component agents with a general predominance of the effect of the dynamic factor. Data on such a dependence are given in Table 3.

Table 3

CONNECTION BETWEEN TYPES OF REACTION TO A COMBINED FORCE AND
THE EFFECTIVENESS OF EACH OF THE FACTORS INDIVIDUALLY

| Type of reaction | Dynamic factor effective at all times | Radiation effective at all times | Dynamic factor weak at all times | Radiation weak at all times | Dynamic factor weak at late periods | Radiation weak at early periods |
|---|---|---|---|---|---|---|
| | Numbers of indices | | | | | |
| I | 1,3,4, 6,7 | 1,2,3, 4,5,7 | 2,5 | 6 | -- | -- |
| II | 7, 9 | 1,2,3, 6,7,8,9 | -- | -- | 1,2,3,4, 5,6,8 | 5,4 |
| IIa | | 1,2 | 1 | -- | 2 | -- |
| III | 3,4 | 2,3,4 | -- | 1 | 1,2 | -- |
| IV | 1,3,4, 5,6,7 | 1,2,4,5, 6,7,8 | 2 | 3 | 8 | -- |
| V | 2,3 | 2,3 | 1,4,5 | 1,4,5 | -- | -- |

Note. Numbers of types of reactions and indices correspond to those in Table 2.

It follows from Table 3 that according to the majority of indices (5 out of 7) the dynamic factor dominates at all times after a combined force (1st type of reaction), when it was effective in individual application. We must note that according to 6 indices out of 7 this type of reaction was observed with high effectiveness of radiation; the latter is reliable according to the criterion of signs ($p < 0.02$).

The second type of reaction (early domination of the effect of the dynamic factor and later that of radiation), according to 7 indices out of 9 was observed when the effectivenss of the dynamic factor was weakened sharply at later periods. According to 7 indices out of 9, radiation was effective at all times. In both cases results are reliable according to the criterion of signs (p<0.05). As reactions of the 1st and 2nd types first proceeded in like manner, we can combine these data. As a result we found that the dynamic factor dominated early according to 14 indices out of 16 when it was effective in individual application and in 13 cases out of 16 when radiation was highly effective. These and other data are reliable according to the criterion of signs (p<0.01).

Therefore, domination of the dynamic factor in a combined force is favored by high effectiveness of the dynamic factor but is not hindered by high effectiveness of radiation. Domination of the radiation effect occurs when the dynamic factor is weakened. The variant of reaction 2a (intermediate position of the effect of a combined force between effects of the joint factors first and domination of radiation later) also follows this principle. In both series of tests of this type the effect of the dynamic factor was weakened either throughout the entire period of the study or at the end.

The third type of reaction (intermediate position of the effect of the /82 combined force between component factors) was noted only in three series of tests according to four indices. In two cases both component factors were effective and in two the action of one or both was weakened. The number of these observations is too small for analysis.

The fourth type of reaction — domination in one subgroup of animals of the radiation effect and in the other that of the dynamic factor — was observed with high effectiveness of the dynamic factor according to 6 indices out of 8 and with high effectiveness of radiation in 7 out of 8. But in this case averaged data cannot be used, as unlike the above described types of reactions, this material was not uniform and is broken down into two different subgroups. Above it was stated that in groups in which the effect of the dynamic factor predominated in a combined force, reaction to a separate force of this factor was clearly pronounced. In subgroups in which the radiation effect dominated, reaction to the dynamic factor was weakened. This theory is

also verified by comparing changes in the unconditioned defense reaction under the influence of acute radiation complicated by two vibrations (see Table 1, series II) with the combined action of ten vibrations and fractionated radiation (see Table 1, series II and VIII).

In the first case the effectiveness of the vibration component was lower and radiation considerably higher than in the second. Evidently, this is why in the first variant of the combined force, domination of the effect of radiation was observed in half the animals and with the second variant the vibration effect dominated in practically all the animals.

Radiation in our tests was ineffective so rarely that at the present time we are not able to study the strength of its effect for type of reaction to a combined force.

The fifth type of reaction — a stable increase of the effect of component factors — we were able to observe only in three series of tests according to 5 indices. In three cases the effectiveness of both combined factors was weak.

Thus, with the combined force of acceleration $(-8g_x)$ for 15 minutes and radiation (3 days later) in a dose of 500 r, the effect on the electric activity of muscles in the afteraction of stimulation of the vestibular analysor was reliably ($p<0.01$) stronger than separate effects of each of the component factors.

The effect of centrifuging alone was unlike the control only in the first 3 days after the force. The effect of radiation alone did not differ from the control according to the criterion of median, revealing reliable differences only according to the criterion of dispersion. The same was also observed in the series of experiments studying the action of vibration and one radiation /83 in a dose of 100 r on conditioned reflexes.

With prolonged food deprivation (18-20 hours) not one of the indices showed visible changes under the influence of separate radiation and vibrations. With joint application of these factors a reliable disturbance was observed in differentiation and a reduction in the strength of the conditioned reflex to Light ($p<0.05$ according to the criterion of comparison of regression series) (Livshits et al., second article in this collection) (see Figs. 4, 5). A completely different picture was seen in experiments on these same animals after brief (4 hour) food deprivation.

In radiated and vibrated rats the conditioned reflex to Tone + increased (p<0.05 and p<0.01, respectively). In rats subjected to a combined force, no reliable differences from the control were found. After radiation and the combined force, the latent period of the conditioned reflex to Light was shortened (p<0.01 and p<0.05). In these experiments, therefore, in not one of the indices was summation of the effects observed.

It is unlikely that the intensification of effects with a combined force against a background of prolonged deprivation of food was caused by over-excitation under the influence of increased motivation and resultant excessive inhibition. If this were so, a reduction in the conditioned reflex to a strong stimulus would rather be expected. It seems more probable that here the weakening of the radiated organism under the influence of starvation was of decisive importance.

Above we noted a variant reaction to a combined force in which strong effects of the joint factors were weakened and weak ones intensified. This phenomenon (also quite rare) verifies that low effectiveness of factors acting separately favors intensification of their effect with a combined application.

Along with this, according to two indices (Table 3, type V), we observed complete summation of the action of the dynamic and radiation factors which were highly effective in separate application. Both these indices were studied in the same series of tests (see Table 1, series IX). One characteristic of these and only these tests was that the rats used were older than those in other studies. It is possible that weakening of protective forces of the body at this age led to the development of type 5 reactions, most severe for the body. Because of the rarity of reactions of the fifth type we were not able to study the conditions determining them.

The effect of the dynamic factor on test indices of the central nervous system created a definite functional background (state of inhibition or excitation) before radiation. Data on the connection between the functional /84 state of the central nervous system immediately before radiation and the type of reaction to a combined force are given in Table 4.

This table shows that no uniform relation could be found between the type of reaction and the functional state of the studied part of the central nervous

Table 4

CONNECTION BETWEEN TYPE OF REACTION AND THE FUNCTIONAL STATE OF A
GIVEN SECTION OF THE CNS IMMEDIATELY BEFORE RADIATION

| Type of reaction | Stimu-lating effect | Inhib-iting effect | No effect on this day | Type of reaction | Stimu-lating effect | Inhib-iting effect | No effect on this day |
|---|---|---|---|---|---|---|---|
| | Numbers of indices | | | | Numbers of indices | | |
| I | 1 | 2,6,7 | 3,4,5 | III | 4,2 | 1,3 | -- |
| II | 1,2,3, 6,7 | 4,5, 8,9 | -- | IV | 1,2,6, 7,8 | 4,5 | 3 |
| IIa | 1,2 | -- | | V | -- | 2,3 | 1,4,5 |

Note. Numbers of indices and types of reactions correspond to those in Table 2.

system during radiation. Type II and III reactions can occur against a background of either the stimulating or inhibiting effect of the dynamic factor. Against a background of the inhibiting effect of the dynamic factor or the absence of its effect, both I and V types of reaction often appear. These conclusions are not definitive. This question requires further study. However, existing material shows that the predominance of stimulation or inhibition in the central nervous system during radiation does not determine the type of reaction. Of decisive importance is the effectiveness of active factors.

In our material we were not able to establish a reliable connection between the type of reaction to a combined force and any of the functional indices. Also no reliable correlation could be established between the type of reaction and parameters of effective factors.

From Table 2 it can be seen that the same indices and kinds of force figure in reactions of different types (the only exception is variant IIa discussed above). From this point of view there are no qualitative differences between the effect of vibration and accelerations. But it must be taken into account that after vibrations, radiations were produced for 5-50 minutes and the interval between applications of accelerations and radiations was 3, 7 and 20 days. Nevertheless, according to several indices the influence of acceleration on the radiation effect was stronger than that of vibration. The fourth

type of reaction (predominance in some animals exposed to a combined force of /85 the radiation effect and in others the effect of the dynamic factor) had a different course when radiation was combined with vibration and acceleration even with the same parameters of radiation force. In the first case the number of animals in which the effect of the dynamic factor predominated was either equal to or less than the number of animals in which the action of radiation predominated. In the second case animals with a predominance of the radiation effect were in the minority. The only exception is index 5 of type 4 (see Table 2). In these tests both subgroups were equal in number, but here radiation occurred 20 days after the dynamic factor.

In reactions of the second type, predominance of the effect of acceleration was more prolonged than that of vibration.

## The effect of dynamic factors on the course
## and outcome of radiation sickness

The literature contains a great deal of material showing that the force of dynamic factors alters the course and outcome of radiation sickness. Various somatic indices have been studied [see 23, 30, 31].

In several cases we also observed a change under the influence of dynamic factors in the effect of radiation on peripheral blood and survival of the animals. These data are given in Table 5.

In comparing Tables 5 and 2 a significant difference appears in the effect of dynamic factors on radiation reactions of the central nervous system and the somatic indices we studied. The former were much more sensitive to dynamic factors. We also observed their reliable and sharp changes in those cases when leukopenic reaction and survival of the animals did not differ from groups exposed only to radiation or the differences were not reliable.

## Several mechanisms of the modifying influence
## of dynamic factors on radiation effects

Acceleration and vibration affect the organism in many ways. Like all stress factors, they affect neuroendocrine regulation, cause strong impulses from peripheral receptors, alter hemodynamics and tissue metabolism.

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Table 5

## THE EFFECT OF DYNAMIC FACTORS ON LEUKOPENIC REACTION
## AND MORTALITY IN RADIATED ANIMALS

| Series | Force | Leukopenic reaction | Length of life | Survival of animals, % |
|---|---|---|---|---|
| I | Radiation 500 r and vibration twice | Unreliable moderation | Unreliable shortening | No effect |
| III | Radiation 600 r and vibration 15 min. before and 24 hrs. after radiation | Moderation ($p < 0.05$) | Lengthening ($p < 0.05$) | Increase ($p < 0.05$) |
| IV | Same | Moderation ($p < 0.01$) | Increase ($p < 0.05$) | No effect |
| V | First vibration 2 min. before radiation. Other conditions see III | No effect detected | No effect detected | No effect detected |
| VI | Prolonged radiation 500 r and vibration twice | Same | Same | Same |
| VIII | Gamma radiation 100 r five times and vibration 30–40 min. before and 24 hours after radiation | Not detected | Not detected | Not detected |
| X | Radiation (50 r) three times. For 3 days before radiation, acceleration —10$g_x$, 8 min. | Moderation ($p < 0.05$) | -- | -- |
| XI | Radiation 500 r. For 3 days before radiation, acceleration —8$g_x$, 15 min. | No effect detected | No effect detected | No effect detected |
| XII | Radiation 500 r. For 7 days before radiation, acceleration —8$g_x$, 15 min. | Unreliable moderation | Unreliable moderation | No effect detected |
| XIII | Radiation 500 r. For 7 days before radiation, acceleration —10$g_x$, 4 min. | No effect detected | No effect detected | Unreliable increase |

Note. Numbers of series correspond to those in Table 1. Not included in this table are series in which few hematological examinations were made.

Therefore, it follows that we should expect mechanisms of the modifying effect of dynamic factors on radiation reactions to be complex and varied.

The first article of L. D. Luk'yanova and L. M. Murashko published in this collection discussed in detail the importance of changes in oxidizing metabolism of nerve tissue in the combined force of vibrations and radiations. The authors showed that the radioprotective effect of vibration (determined by indices of survival and leukopenic reaction) is connected with postvibration depression of oxidizing processes.

Earlier tests in vivo established that vibrations affect two-phase changes in oxidizing metabolism in brain tissues. The start of vibrations is accompanied by a reduction of oxygen pressure in brain tissue and its increased utilization against this background. In the postvibration period this phase was replaced by a phase of depressed oxidizing processes, reaching a maximum 10-20 minutes after vibration stimulation. Therefore, in rats radiated 15 minutes after vibration, radiation sickness was much lighter and mortality /87 was lower than in rats exposed to radiation only. In the first of these groups, 30% died and in the second, 90% ($p < 0.5$). This also gave rise to the assumption that the initial state of oxidizing metabolism in the nervous system is of decisive importance in the development of radiation damage [27].

The work of L. D. Luk'yanova and t. M. Murashko, published in this collection, in tests in vitro verified that vibration causes phase changes in oxidizing metabolism in nerve tissue.

Metabolic processes in tested sections of the brain increased during the first minutes of vibration. This phase was then replaced by depression of oxidizing processes, reaching a maximum 15 minutes after termination of the force. With the combined force of vibration and radiation the effect of radiation produced 3-5 and 15 minutes after vibration was ambiguous.

When the animals were radiated 15 minutes after vibration against a background of maximum depression of oxidizing processes, radiation sickness was much milder than in animals radiated 2 minutes after vibration, i.e. when postvibration inhibition had not yet developed.

There is basis for thinking the protective force of postvibration inhibition is connected with general repression of oxidizing processes, as tissue respiration in peripheral organs was inhibited at the same time [28].

We suggest that tissue hypoxia is significant in the modifying influence of accelerations on radiation effects.

According to our observations, in animals (rabbits, rats, dogs) exposed to accelerations ($-g_z$ and $-g_x$) there are changes in the temperature of the brain which are stereotyped in all cases. At the start of the force there is a brief (0.5-1.5 min.) rise in temperature which then, regardless of the length of exposure, changes to a prolonged (20-30 min.) temperature drop [13]. As would be expected, a similar temperature reaction could be reproduced at least qualitatively by hypoxia. The development of a hypoxic condition in the brain (and not only in the brain) with accelerations can today be considered an established fact [14, 15, 16]. This is the result of disturbances of hemodynamics and external respiration [5, 7, 10, 18, 19, 34]. Severe reduction of regional arterial flow in our experiments with accelerations of $+g_z$ appeared as a special phase of the temperature reaction in the sensorimotor cortex in rabbits [11, 12, 13]. In experiments with hypoxia, animals were given oxygen-poor mixtures to breathe which contained 10.5 or 0.2% $O_2$ in $N_2$ /88 at atmospheric pressure. The duration of hypoxia was the same as that of acceleration in preceding tests (30-180 sec.). It was found that temperature changes in the sensorimotor cortex of the rat and rabbit accompanying acute hypoxia are analogous to those observed with accelerations. Thus, there is reliable basis for assuming that during acceleration an oxygen and substrate deficit is created which can later be compensated physiologically. The temperature drop, being the first part of the reaction to acceleration and hypoxia, evidently, coincides with the phase of increased excitability in tested structures of the brain. This theory is verified by data obtained in motoneurons of the spinal cord during acute hypoxia [35]. Electroencephalographic data indicate generalized excitation in the cortex, subcortex and reticular formation in animals during the initial period of acceleration [6, 9]. Therefore, a paradoxical situation arises in which extremely high activity of several structures, by itself accompanied by increased heat production, develops with the increasing energy deficit. Under these stress conditions the respiratory chain of the cell functions abnormally; the number of points of connection is reduced [32], but the dispersal of energy in the form of heat increases. This factor is possibly responsible for the main part of increased heat production

in the first phase of the temperature reaction to acceleration. This state
is maintained until the energy resources of the tissue are exhausted to that
minimum when the concentration of oxygen in the tissue becomes the regulator
of the intensity of energy metabolism [1]. Then there is a reduction in the
consumption of oxygen, maintained for a short time when normal air is supplied
for breathing or when acceleration stops. The after-action period corresponds
to the period of deep depression of the amplitude of spikes of monosynaptic
responses after acute hypoxia [35] and in accordance with electroencephalo-
graphic data, to the period of inhibition after accelerations [6, 9]. From
this it follows that accelerations cause a very significant shift in energy
exchange in the central nervous system. Changes of this type are accompanied
by slowly diminishing fluctuations in the excitability of individual links in
the central nervous system, the concentration of corticosteroids, catechol-
amines in the blood and tissues, etc. It is evident that the total effect of
a combined force will depend primarily on the phase of these fluctuations when
a certain dose of radiation is produced. We observed only two phases of this
process in its temperature expression; the first of these had, as noted, a
period 30-60 times shorter than the second. It is possible that subsequent
fluctuations are even longer, as involved in the cycle are systems responding to /89|
the energy exchange of the organism as a whole, for example, the system of
thermoregulation. Our hypothesis is that hypoxic stress during accelerations
is the primary mechanism triggering the damping fluctuation process in the
organism, whose phase significantly affects radiosensitivity.

## Discussion

The effect of nonradiation factors on the course and outcome of radiation
sickness has been widely studied according to various indices in recent years.
Many authors have come to the conclusion that the most important mechanism in
the modification of the radiation effect is change in nonspecific resistance.
Some literature data on this question are given in the introductory article of
N. N. Livshits in this collection. We feel that this mechanism is very im-
portant in the effects we discovered of the combined force of dynamic factors
and ionizing radiation.

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Along with this the specific influence of vibration on radiation effects was also observed. Radioprotective action of vibration alone appeared against a background of postvibration depression of oxidizing metabolism.

Although the depression of exchange processes takes part in the effect of many factors on radiobiological reactions, this effect can, evidently, be considered specific for vibration. We came to this conclusion because the alternation of phases of oxidizing metabolism which we observed occurred several minutes after the termination of vibration, which does not fit into the scheme of the adaptation syndrome. However, neither this mechanism nor the phenomenon of cross resistance give a comprehensive explanation of the reactions of the central nervous system to combined forces.

In the introductory article are given facts showing that regularities of the combined effect of dynamic and radiation factors on the central nervous system cannot be completely explained by changes in nonspecific resistance. These data can be supplemented by the following proofs.

1. Nonspecific resistance is weaker than specific [36]. In our tests the first was extremely strong, often leading to complete masking of the radiation effect, but specific resistance, created by vibration forces, was not clearly expressed. This is verified by tests in which the vibration force was applied repeatedly; 24 hours after the first vibration, reaction to this force| did not change sharply [28].

2. The phenomena of cross resistance and the specific radioprotective /90 effect of dynamic factors are mechanisms affecting the radiation reactions of many systems of the body, not only the central nervous system. At the same time, differences between the combined effect of the factors we applied on functions of the central nervous system and on reactions of the blood system and the course and outcome of radiation sickness are very great . This applies not only to the quantitative difference shown in Table 5. According to somatic indices the radiation effect always dominated in cases of combined forces. The effect of the dynamic factor only modified reactions to radiation. Even when acceleration was combined with radiation in comparatively small doses (Table 5, Series X) the leukopenic reaction was only slightly weakened. In series III and IV when the radioprotective action of vibration was clearly expressed, all typical traits of radiation sickness were maintained. This completely agrees

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with literature data [see 23, 31].

Radiation reactions of the central nervous system with such forces were essentially altered, often took the opposite direction and became entirely indistinguishable.

Of decisive importance for the results of the combined effect on somatic indices was the general condition of the animals during radiation as well as characteristics of energy indices.

Thus the radioprotective effect of vibration in our tests appeared only when radiation was conducted against a background of postvibration inhibition of oxidizing processes in tissues. In the central nervous system an identical force caused different types of reaction in the same animals according to different indices. Thus, as the result of radiation three days after centrifuging, type 2, 4 and 5 reactions were recorded in the system of the vestibular analysor, i.e. both radioprotective and aggravating the radiation effect. In addition, the predominance of stimulation or inhibition during radiation in structures responsible for a given function also had no decisive importance for the type of reaction. We found no indications of uniform dependence of the type of reaction on intensification or weakening of the functional activity of a given system under the influence of the preliminary force of dynamic factors. True, the 5th type of reaction was never observed after radiation conducted against a background of increased functional activity. But even the 1st type was very rarely (only once) observed against a background of the stimulating effect of the dynamic factor, although there is a sharp difference between reactions of the 1st and 5th types.

In reactions of the 4th type domination of the effect of acceleration and radiation was noted in the same direction as that of the dynamic factor. The action of the latter differed only quantitatively.

The literature includes data on the dependence of the effect of radiation    /91
on the central nervous system on the functional state of the latter [8,33]. We suggest that such a sharp dependence is absent in our experiments because radiation reactions of the central nervous system in this case were affected by other, stronger factors. That we did not find a uniform dependence of the type of reaction of the central nervous system to a combined force on its functional state during radiation can be partially explained by the fact that the

leading role in a combined effect is played by the dynamic factor.

This is verified by the material discussed above. In addition, it can also be indicated that in reactions of the 4th type there was no connection established between the predominance of the radiation effect in the combined action on a tested function of the central nervous system and the severity of radiation sickness, determined by leukopenic reaction and times of death [24]. All this indicates that reactions of the central nervous system to a combined force are relatively autonomous. From this it can be assumed that there are possibly various mechanisms of the combined action of radiation and dynamic factors on functions of the central nervous system and on somatic indices. It can also be assumed that these differences are connected with mechanisms inherent only to the central nervous system. One of these mechanisms can be the interaction of nerve processes, caused by various stimuli. Along with the effect on primary radiobiological reactions, dynamic factors which are universal for the entire organism also act on basic nerve processes. Under the influence of radiation there are significant changes in the condition of nerve centers [22]. Vibrations and accelerations cause a powerful flow of impulses from the periphery, also altering the functional state of the central nervous system. The reactions we have discussed can be the result of the interaction of these influences. Dynamic factors, acting before radiation and appearing as weak stimuli of the central nervous system, can create dominant foci in it, repressing stimulating or inhibiting processes caused by later radiation (reaction of the first type). When effects of the dynamic factor diminish, the dominant fades and radiation effects set free because of its influence (reaction of type 2 and 2a) become evident.

Necessary for the creation of a dominant focus is the stimulation of a sufficiently large force. Therefore, the dominant focus appears only in animals with a strong reaction to the dynamic factor; in animals with a weak reaction, only the effect of radiation appears (reaction of the 4th type). If the stimuli have a weak effect on the central nervous system dominant foci cannot develop and inhibition caused by each of the agents is not suppressed but summarized.

This also occurs in a weakened organism (reactions of the 5th type). /92
Such effects are possible for stimulating processes, but we still have not ob-

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served increased functional activity with reactions of the 5th type. The concept of the intracentral localization of the interaction of reactions to radiation and dynamic factors also agrees well with our idea of the causes for increasing weak and weakening strong effective factors, sometimes observed in the same experiment. These phenomena are connected with changes in the functional state of the central nervous system when corresponding values of the reaction and the strength of the stimulus are disturbed.

From these theories it also becomes understandable why|the functional state of the central nervous system during radiation does not have decisive importance for the results of a combined force, but the conditions under which functions of the central nervous system of animals were studied sometimes completely determined these reactions (the effect on the combined action of vibration and radiations of the length of food deprivation before the day of the conditioned reflex study).

This scheme was suggested to us by the monograph of G. I. Kositskiy and V. M. Smirnov [17]. The authors of this monograph assume as a working hypothesis the explanation of nonspecific resistance by the mechanism of the dominant created in the central nervous system by the effect of a nonspecific stimulus and suppressing pathological processes.

Here we are not considering this hypothesis as a whole, but feel that under the conditions of our studies, when we were concerned with end processes developing in the central nervous system, the mechanism of the dominant is very probable.

At the present time we have no direct proofs that the mechanism of the dominant is of decisive importance in the phenomena we observed instead of processes with only external similarity. But the assumption we have voiced agrees highly with all facts which we have available indicating this hypothesis is probable. We do not assume that the mechanism of the intracentral inter-action is the only mechanism in the effects we have observed. The specific action of the dynamic factor and neurohormonal regulation of resistance also play a role. The latter, probably, ensures the length of the after-action of dynamic factors. But the|regularities we have described most often corres-pond to the theory of the intracentral interaction of the effects of dynamic factors and radiation. Therefore, in accordance with the still only working hypothesis we suggest this mechanism be considered the most important one.

REFERENCES

1.  Alyukhin, Yu.S.  Fiziologicheskiy zhurnal SSSR, No. 54, 1968, p. 998.          /93

2.  Apanasenko, Z.I.  In the book:  "Vliyaniye ioniziruyushchikh izlucheniy i
    dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The
    Effect of Ionizing Radiations and Dynamic Factors on Functions of the
    Central Nervous System).  Moscow, "Nauka", 1964, p. 92.

3.  Apanasenko, Z.I.  In the book:  "Vliyaniye faktorov kosmicheskogo poleta
    na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight
    Factors on Functions of the Central Nervous System).  Moscow, "Nauka",
    1966, p. 218.

4.  Apanasenko, Z.I.  In the book:  "Nekotorye voprosy kosmicheskoy neyro-
    fiziologii" (Some Questions of Space Neurophysiology).  Moscow, "Nauka",
    1967, p. 184.

5.  Barer, A.S.  Kosmicheskaya biologiya i meditsina., No. 1, 1967, p. 57.

6.  Barer, A.S. and V.B. Zubavin.  In the book:  "Problemy kosmicheskoy biologii"
    (Problems of Space Biology).  Moscow, "Nauka", No. 4, 1965, p. 349.

7.  Barer, A.S. and Ye.A. Sokol.  Kosmicheskaya biologiya i meditsina., No. 5,
    1971, p. 55.

8.  Grigor'yev, Yu.G.  Vestnik rentgenologii i radiologii., No. 2, 1956, p. 3.

9.  Izosimov, G.V. and A.N. Razumeyev.  In the book:  "Problemy kosmicheskoy
    biologii" (Problems of Space Biology).  Moscow, Izd-vo AN SSSR., No. 2,
    1962, p. 247.

10. Kiselev, A.A.  In the book:  "Problemy kosmicheskoy biologii" (Problems
    of Space Biology).  Moscow, Izd-vo AN SSSR, No. 2, 1962, p. 231.

11. Klimovitskiy, V.Ya.  In the book:  "Vliyaniye ioniziruyushchikh izlu-
    cheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy
    sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on
    Functions of the Central Nervous System).  Moscow, "Nauka", 1964, p. 33.

12. Klimovitskiy, V.Ya.  In the book:  "Vliyaniye faktorov kosmicheskogo
    poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space
    Flight Factors on Functions of the Central Nervous System).  Moscow,
    "Nauka", 1966, p. 11.

13. Klimovitskiy, V.Ya. Krovosnabzheniye i temperatura golognogo mozga zhivotnykh v usloviyakh deystviya na organizm uskoreniy (The Blood Supply and Brain Temperature of Animals Under the Influence of Accelerations). Author's abstract of candidate's dissertation, Moscow, 1968.

14. Kovalenko, Ye.A., V.L. Popkov and I.N. Chernyakov. Fiziol. zhurn. SSSR, No. 49, 1963, p. 719.

15. Kovalenko, Ye.A., V.L. Popkov and I.N. Chernyakov. Voyenno-med. zhurn. No. 5, 1964, p. 81.

16. Kovalenko, Ye.A., V.L. Popkov and I.N. Chernyakov. Izvestiya AN SSSR, Biology series, No. 3, 1964, p. 376.

17. Kositskiy, G.I. and V.M. Smirnov. Nervnaya sistema i stress (The Nervous System and Stress). Moscow, "Nauka", 1970.

18. Kotova, E.S., L.A. Kitayev-Smyk and B.V. Usyushkin. Kosmich. biol. i med. No. 5, 1971, p. 42.

19. Kotovskaya, A.R., S.I. Lobashkov, S.F. Simpura, P.M. Suvorov and G.F. Khlebnikov. In the book: "Problemy kosmicheskoy biologii" (Problems of Space Biology). Moscow, Izd-vo AN SSSR., No. 2, 1962, p. 238.

20. Kuznetsova, M.A. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 122.

21. Kuznetsova, M.A. In the book: "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 93.

22. Livanov, M.N. Nekotorye problemy deystviya ioniziruyushchey radiatsii na nervnuyu sistemu (Some Problems of the Effect of Ionizing Radiation on the Nervous System). Moscow, Medgiz., 1962.

23. Livshits, N.N. In the book: "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1964, p. 5.

24. Livshits, N.N., Z.I. Apanasenko and Ye.S. Meyzerov. Radiobiologiya., No. 9, 1969, p. 46.

25. Livshits, N.N. and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 236.

26. Livshits, N.N., Ye.S. Meyzerov, R.M. Zakirova and V.A. Tikhaya.  In the book:  "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space Neurophysiology).  Moscow, "Nauka", 1967, p. 169.

27. Luk'yanova, L.D.  In the book:  "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy" (The Effect of Ionizing Radiations and Dynamic Factors on Functions of the Central Nervous System).  Moscow, "Nauka", 1964, p. 145.

28. Luk'yanova, L.D.  Okislitel'nyy metabolizm i reaktivnost' nervnoy tkani      /94
v perezhivayushchikh preparatakh i v usloviyakh tselostnogo organizma (Oxidizing Metabolism and Reactivity of Nerve Tissue in  Surviving Specimens and in the Intact Organism).  Author's abstract of doctoral dissertation.  Moscow, 1971.

29. Luk'yanova, L.D., A.V. Kol'tsova, Ye.S. Meyzerov and Ye.P. Kazanskaya.  In the book:  "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System).  Moscow, "Nauka", 1966, p. 105.

30. Rayeskaya, S.A. and Yu.G. Grigor'yev.  In the book:  "Deystviye protonov vysokikh energiy" (The Effect of High Energy Protons).  Moscow, Atom-izdat., 1967, p. 71.

31. Saksonov, P.P., V.V. Antipov and B.I. Davydov.  Ocherki kosmicheskoy radiobiologii (Outlines of Space Radiobiology).  Moscow, "Nauka", 1968.

32. Skulachev, V.P.  Akkumulyatsiya energii v kletke (The Accumulation of Energy in the Cell).  Moscow, "Nauka", 1969.

33. Sokolova, N.V.  Rol' funktsional'noy nagruzki v likalizatsii luchevogo povrezhdeniya (The Role of Functional Load in the Location of Radiation Damage).  Tomsk.  Izd-vo Tomsk. gos. un-ta., 1962.

34. Banchero, N., L. Cronia, A.C. Nolan and E.H. Wood.  Aerospace Med. No. 36, 1965, p. 608.

35. Piwonka, R.W. and C.D. Barnes.  J. Applied Physiol. No. 29, 1970, p. 96.

36. Selye, G.  The Physiology and Pathology of Exposure to Stress.  Montreal. Medical Publ., 1950.

# II
## MECHANISMS OF THE EFFECT OF ACCELERATIONS
## AND VIBRATION
## ON THE CENTRAL NERVOUS SYSTEM

### SOME CHARACTERISTICS OF HYDROSTATIC
### PRESSURE DISTRIBUTION IN THE VASCULAR SYSTEM
### DURING ROTARY ACCELERATIONS

V. Ya. Klimovitskiy, G. L. Pastorye

Changes in the distribution of the hydrostatic pressure of the blood during accelerations are|considered one of the essential factors in circulatory disturbances. It is known that the pressure distribution curve along the length of the vascular hydrostatic column, reflecting the state of acceleration in time, passes through a point corresponding to the initial pressure (before the force). According to Gauer (1963), the concept of a hydrostatically indifferent point (HIP) as applied to the vascular system [11] was developed by Blumberg (1885) and Wagner (1886). Actually regularities in pressure distribution during accelerations were studied quite thoroughly even earlier by V. V. Pashutin [6] who published his data in "Lektsiyakh obshchey patologii" (Lectures on General Pathology) (1881). In model tests and in experiments on dogs V. V. Pashutin obtained all basically important ratios and correctly explained them qualitatively. After a brief interruption in studying these phenomena, attention was again directed toward them in the 1930s in connection with the development of aviation medicine when Clark et al. (1934) provided the simplest formula connecting the location of a hydrostatically indifferent point with indices of the elasticity of the walls of the vascular system [9]. Later, in the 1950s and 1960s, during intense research in the field of space physiology and, in particular, the effect on the body of acceleration, researchers again turned to laws of pressure distribution in a closed system

and the concept of a hydrostatically indifferent point. In particular, during this period a number of studies experimentally established the location of a point of constant pressure during change in body position in relation to the vector of gravity and with various directions and conditions of acceleration [10, 13, 15, 22]. These data as well as elementary theoretical information are generalized in surveys [4, 12].

B. M. Savin (1970) turned his attention toward the discrepancy between the theoretical value of hydrostatic pressure and that obtained experimentally (the empirical value is less than theoretical). Subject to criticism is the point of view according to which hydrostatic pressure in the vascular system can be represented as the weight of the entire hydrostatic column above the point of measurement [7].

In these studies the factor of nonuniformity of the vector field, typical of rotary acceleration, was not taken into consideration. The purpose of this work is to analyze several characteristics of accelerations, taking this factor into account. The authors are aware that it is hard to expect significant new results in the traditional field of physiology with which these questions are concerned. Nevertheless, it is of interest to find out which special consequence will result, for example, from using a centrifuge with a relatively small radius. The concept of "small" in this case requires more precise definition. In any radius of rotation R there is a drop in effective acceleration G (in units of the acceleration of gravity $g_0$), depending only on angular speed $\omega$:

$$\frac{dG}{dR} = \frac{\omega^2}{g_0}. \tag{1}$$

By "length of the object" let us understand its projection (h) onto the radius so that $h = R_2 - R_1$. Then the total acceleration drop in the object is

$$\Delta G = \frac{\omega^2}{g_0}(R_2 - R_1). \tag{2}$$

So that in giving the required acceleration $G_n$ to the object the value of $\Delta G$ is as small as possible, we must try to create the lowest angular speed

because of the increase of radius R:

$$\frac{dG}{dR} = G_n \frac{1}{R_n} .$$

(3)

Derivative dG/dR is not an adequate criterion for estimating nonuniformity as the total drop $\Delta G$ depends more and more on the length of the object. The criterion of nonuniformity can be $\Delta G/G_m$, where $G_m$ is acceleration at the mid-point of the object $R_m$, notably:

$$q = \frac{\Delta G}{G_m} = \frac{R_2 - R_1}{R_m} .$$

(4)

As applied to the biological action of accelerations, the basis for the qualification of nonuniformity according to criterion q as "large" or "small" should be some physiological effect dependent upon the factor of non-uniformity. The same also applies to estimating the value of $R_m$ as "relatively small." Some frequent examples will be discussed later. The value of q, typical of cases often encountered in experiments, could be estimated approximately beforehand: $\pm G_z$ accelerations on a centrifuge with a radius of 3-4 m, length of the objects 0.2 m (small laboratory animals) to 0.8 m (large dogs). Accordingly, q will be between 5-27%. These are values of q for medium centrifuges usually used in studying acceleration in animal experiments. Strict evaluation of the results requires calculation of those differences which are introduced by the factor of nonuniformity. Similar demands must be made of analysis of the results of experiments with "artificial gravity" in weightless conditions if the radius of rotation of the on-board unit can be considered small. Finally, there is special interest in pressure distribution in cases of rotation around an axis running through the body. Such a phenomenon could arise, for example, in cases of ejection.

The hydrostatically indifferent point should probably not be considered only as a formal parameter of the pressure distribution curve and be treated as some arbitrary reference level. The initial level of pressure, to which a given point corresponds and conforming with tissue and intraorgan pressure, determines (with stable conditions) whether the vascular channel will be dilated or contracted (up to closure of the vessels) "above" or "below" this point. Its

location could be found by using the formula given by Clark et al. [9]

$$a = h \frac{E_1}{E_1 + E_2},$$ (5)

where  a  is the length of the "upper" part of the hydrostatic column, h  is its total length, $E_1$ and $E_2$ are coefficients of elasticity of "upper" and "lower" parts, respectively:

$$E = \frac{dP}{dV},$$ (6)

where dP is the change in pressure and dV the change in volume.

In a uniform force field pressures in the "upper" and "lower" parts of a closed hydrostatic column for an object positioned horizontally:

$$P = d_1 G (R_2 - R_1) *.$$ (7)

In a nonuniform field during rotary acceleration at radius R we have:   /98

$$E = k \frac{1}{\Delta V} (R_n^2 - R_i^2),$$ (8)

where $R_n$ is some point of the radius, $R_i$ is the radius of rotation of the HIP ($R_2 > R_i > R_1$).

As a result the dependence of the location of the HIP on radii of rotation of extreme points of the hydrostatic column $R_1$ and $R_2$ is:

$$R_i = \sqrt{(R_2^2 - R_1^2) \frac{E_1}{E_1 + E_2} + R_1^2}.$$ (9)

Pressure in such a system is distributed parabolically:

$$P = d_1 (R^2 - R_i^2) \frac{\omega^2}{2g_0}.$$ (10)

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*$d_1$ — specific gravity of liquid.

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Let us find the physiological result of such pressure distribution as compared with that occurring in a uniform force field. In previous tests [2, 3] an object with a length $h = R_2 - R_1 = 40$ cm (rabbit, dog weighing 5-6 kg) was rotated with acceleration at the midpoint equal to $+6.34$ $g_z$. Let us consider the following conditions: 1) $R_1 = 0$; 2) $R_1 = 50$ cm; 3) $R_1 = 350$ cm; and 4) $R_1$, $R_2 \to \infty$ (object significantly removed from the center of rotation so that $h << R_m = \dfrac{R_1 + R_2}{2}$ , but $R_1$ and $R_2$ have finite values). In the first case the upper point of the hydrostatic column is directly at the center of rotation. Point (2) corresponds to the conditions of our test. Point (3) meets conditions when distance from the center of rotation is sufficient for practically even distribution of acceleration in the object of the given dimension (q=11.4%). For point (4) let us say that dG/dR=0.

Let us assume that in all four cases acceleration at the midpoint of the object $R_m$ is the same and to meet this requirement let us appropriately select angular speed:

$$\omega = \sqrt{\frac{G_n g_0}{R_m}} .$$ 
(11)

Using formulas (7), (10) and (11) it is easy to show that the total pressure drop depends only on the length of the object and on acceleration and when condition (11) is fulfilled it will be steady. Later, on the basis of (7), (10) and (5) it follows that pressures $P_1 = P(R_1)$ and $P_2 = P(R_2)$ in meeting the requirements of (11) coincide, respectively, for linear (7) and parabolic (10) distributions. Then graphs of pressure distribution by volume, corresponding to points 1-4, have the shape shown in Fig. 2. The location of points $P_1$ and $P_2$ on the axis of ordinates is determined by a reference system. It can be absolute (atm., $g/cm^2$, mm Hg, etc.) or relative.

To estimate the maximum physiological effect connected with the difference between uniform and nonuniform fields, let us analyze the case when the level of $P_1$ passes through the area of greatest divergence between distribution curves. For this let us assume that point $R_i$ is 1/3 the length of the object from the central end, which we shall assume is the head. As will be evident from the following, the position of $R_i$ taken here corresponds to the region of the probable location of the HIP in actual conditions.
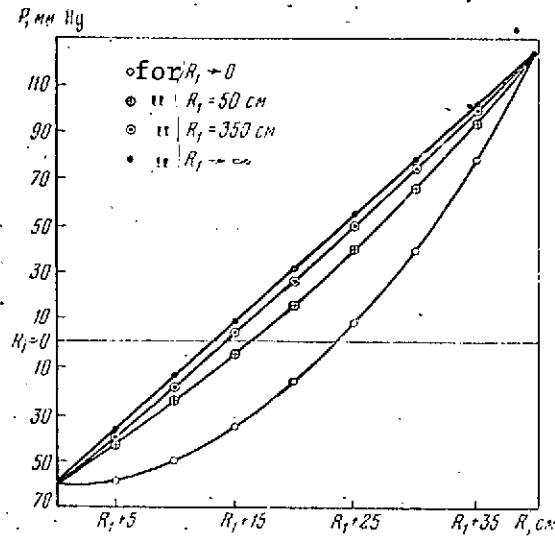
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Figure 1. Hydrostatic pressure distribution in a closed system in relation to the radius of rotation.

Horizontally — radius of rotation of the object's closest point to the center ($R_1$); vertically — pressure (in mm Hg) reckoned from the original value (before rotation), taken as zero.

Let us consider distribution curves given in Figure 1. Other conditions being equal, the location of the hydrostatically indifferent point depends on the slope of acceleration drop. Notably: with increased dG/dR the value $R_i$–$R_1$ rises in a nonuniform field, i.e. the HIP shifts to the side of the overload vector (opposite to the direction of the acceleration vector). For an object of the given length there is a difference limit of the abscissas h; the minimum value $R_i$ corresponds to case (4), the maximum, to case (1). Therefore, with the given $R_1(G_n)$ the shift of the HIP compared with a uniform field is a constant. In particular, in our case in a uniform field when $G_n$=6.34, h=40 cm, $R_i$— $R_1 \cong 0.3$ h, maximum shift is ~ 10.5 cm. The difference between the conditions of our test and case (4) is evaluated by the shift of $R_i$ on the order of 3 cm and compared with conditions of a test on a centrifuge with a radius of 3.5 m the shift is 2 cm.

Let us turn to analyzing $\dfrac{E_1}{E_1+E_2}$ . Volumetric expansion coefficients $E_1$ and $E_2$ can vary formally from 0 to $\infty$ and the value $a = \dfrac{E_1}{E_1+E_2}$, from 0 to 1. Therefore, $R_i$ can assume values from $R_1$ to $R_2$. It is evident that the shift

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of the hydrostatically indifferent point corresponds to transference of the origin (along the ordinate) and does not affect the form of function P=P(R).

In the case of +G$_z$ acceleration increased tension of the walls of the hydrostatic column in its "lower" part (increase of coefficient E$_2$), other conditions being equal, causes a shift of point R$_i$ toward the center of rotation counter to the overload vector. Ordinates P(R) merge upward by the quantity

$$\Delta P = -\frac{\omega^2}{g_0} \Delta (R_i^2) \cdot$$

(12)

Therefore, if the same mechanical energy is imparted to the object by creating the same linear or rotary acceleration at the midpoint, then in the latter case the distribution of pressure and volumes is different, notably: HIP is shifted toward the overload vector. At the same time the location of this point is, evidently, not indifferent for the organism. According to experimental data, in a man changing from supination to a vertical position with the head up, the point is 9 cm below the diaphragm [13]; with the head down — in man and dog the HIP is located at the front in the right auricle, slightly closer to the head [15, 22]. The same location of the HIP can also be found according to indirect indices; not only in transferring to a vertical position but also with +G$_z$ acceleration: with + 6 G$_z$ HIP is located about 10 cm below the upper descending aorta in monkeys [16] and in man at –2 G$_z$ in the area of the heart [14, 17].

On the basis of these facts, it can be assumed that in changing from supination to a vertical position with the head up and with +G$_z$ accelerations HIP is located "above" the level of 0.5 h (closer to the head). When the sign of the force is changed (–G$_z$), this point is shifted even more toward the head. In general we can make the following conclusion: in the living organism the HIP is located near the heart so that this organ is in a zone of reduced pressure (as compared with the original). One interesting detail calls attention to itself. If the above facts are true, then with +G$_z$ $\frac{E_1}{E_1+E_2}$ < 0.5 and with –G$_z$ we have $\frac{E_1}{E_1+E_2}$ > 0.5, i.e. HIP is determined in a certain zone by the redistribution of vascular tone in the "upper" and "lower" parts of the vascular

channel. Such a correlation occurs only in a living organism and is due, probably, to the heart's need to be in an area of relatively low pressure.

Thus, compared with linear acceleration, rotation given the same energy is a more serious factor, as attaining a certain distribution with rotary acceleration requires some additional work, as the result of which pressure in the system must increase by $\Delta P$. Then the distribution parabola shifts to the left, passing through $R_1$. Work performed is expressed as

$$\Delta A = \Delta P \cdot \Delta V \qquad (13)$$

The order of magnitude of $\Delta A$ can be determined. For the above case (2) (see Figure 2) $\Delta P \cong 15$ mm Hg. Assuming that $\Delta V$ is on the order of $n \cdot 10^{-1}$ l (no more), where $n < 5$, we obtain

$$\Delta A = \Delta P \cdot \Delta V = 15 \text{ mm Hg} \cdot n \cdot 10^{-1} \cong$$
$$= 2n \cdot 10^{-1} \text{ J}.$$

Taking into account that the efficiency of smooth muscles ~ 25%, we obtain $\Delta A$ on the order of ~ n J. Energy expenditures of this order comprise the difference between work for cases (4) and (2) with h=0.4 m, i.e. for a rabbit or small dog. If analogous changes of volumes are 10 times greater in man, then the additional expenditure of energy does not exceed several tens of joules. This is very little work for the final effector link but it is performed with the participation of peripheral and central control systems. As applied to these links of the reaction it would be difficult to estimate the additional energy expenditure connected (in the final analysis) with a difference in initial volume shifts. But we must take into account that with $\pm G_z$ accelerations on the order of 2-5 g in hypoxic conditions of hemodynamic origin even a small additional energy load takes greater effort and, evidently, always at the expense of other functions not at that moment vitally important. Could it be that under these conditions the cardio-vascular system and regulating mechanisms do the necessary work whose index is a shift in pressure $\Delta P$?

As has been shown, during acceleration there are rather rapid compensation pressure changes in the body on the order of those required to move the HIP to /102 the necessary location. Thus, during acceleration $(+G_z)$ pressure in the area

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of the head is restored to 60 mm Hg in 12-15 seconds after exposure [21].
According to Sicker [20], under these conditions there is a rise in arterial
pressure of 5 mm Hg per g [20]. According to other authors [8, 19], there is
a simultaneous active increase in venous tone. According to Britton [8],
venous pressure in the vena cava of dogs actively increases 50-100% during $^{-G}z$
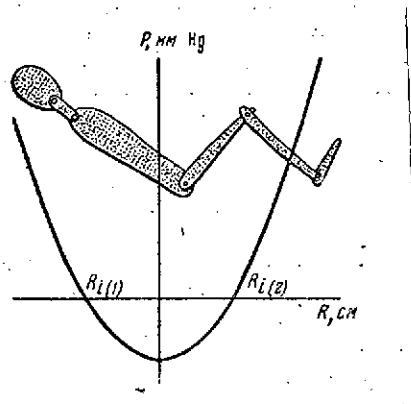acceleration. Under physiological conditions, therefore, the organism, evi-



Figure 2. Hydrostatic pressure distribution in the human vascular system
during rotation around an axis passing through the body. This represents
distribution before any break in the hydrostatic column and under conditions
of symmetric distribution of two hydrostatically indifferent points.

dently has available to it resources for recovering necessary pressure ratios
in case of $+G_z$ accelerations on the order of several g. At the same time the
shape of the pressure distribution curve remains unchanged (linear dependence
for a uniform field and a parabola for rotary acceleration). There is a shift
in the distribution curve in the coordinate system rigidly connected to the body.
This shift occurs with corresponding changes in vascular tone.

From this it follows that other conditions being equal, rotary acceleration,
at least according to pressure distribution indices, is linked with greater
energy expenditures which are, generally speaking, quantitatively calculable.

There is great theoretic interest in the case of rotation around an axis
passing through the body. Under these circumstances pressure, evidently, can-
not be distributed other than parabolically. Figure 2 shows the distribution
curve of the static component of pressure for the vascular system of a man
rotated around an axis passing approximately through the center of gravity.

As (on the basis of the preceding | analysis) the maximum difference of pressures
for each rotating "half" of the body is constant, functional continuity at the
point of minimum must be provided by certain additional conditions. Notably:
in this case the coefficients of elasticity must "fit" so that the location of
the two indifferent points formed under these conditions will correspond to
parabolic distribution. Otherwise with sufficient angular speed a |
break in the hydrostatic column is inevitable at the point of minimum pressure,
after which the two resultant systems can behave independently. It |
is clear that this condition indicates a complete breakdown of blood circulation. |
Conditions when such a break can occur can generally be determined.

For calculation let us use a model in which the blood conveying system is
considered as a closed elastic pipe (unlike Clark's model where two elastic
volumes were connected with a rigid pipe).

Liquid with volume V is in a straight horizontal pipe with length of
$h = h_1 - h_2$. Cross section S(x) of the pipe at each point x with $h_1 < x < h_2$
depends linearly on the difference between the pressure of the liquid in the
pipe $P_i = P(x)$ and external (atmospheric) pressure $P_e$:

$$S(x) = S_0 + R[P(x) - P_e] = S_0 + KP_\Delta(x).$$ 

(14)

For simplicity let us assume that $S_0$, i.e. the cross section of the pipe with
$P_e = P_i$, coefficient k connecting pressure $P_\Delta(x)$ and the cross section of the
pipe at point x, do not depend on x. Rotation proceeds around a vertical axis,
passing through point x = 0, with angular speed $\omega$. According to (10), pressure
P(x) here is equal to P(0) = + $\omega^2 d_1/2g_0$ $x^2$. The volume of liquid in a rotating
pipe is

$$V_1 = \int_{-h_1}^{h_2} S(x)\,dx = \int_{-h_1}^{h_2} \left\{ S_0 + k\left[ P(0) + \frac{\omega^2 d_1}{2g_0} x^2 - P_e \right] \right\} dx =$$
$$= (h_1 + h_2)[S_0 + kP(0) + kP_e] + k\frac{\omega^2 d_1}{6g_0}(h_1^3 + h_2^3).$$

(15)

In a stationary pipe, when P(x) is identical to $P_0$, the average pressure of
the liquid, its volume is

$$V_2 = \int_{-h_1}^{h_2} [S_0 + k(P_0 - P_e)]\,dx = (h_1 + h_2)(S_0 + kP_0 - kP_e).$$

(16)

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As the volume of the liquid remains constant, from (15) and (16) we have

$$V_1 = V_2 = (h_1 + h_2)\,[S_0 + kP(0) - kP_e] + k\frac{\omega^2 d_1}{6g_0}(h_1^3 + h_2^3) =$$
$$= (h_1 + h_2)(S_0 + kP_0 - kP_e),$$

from which

$$P(0) = P_0 - \frac{\omega^2 d_1}{6g_0}(h_1^2 - h_1 h_2 + h_2^2). \tag{17}$$

A break occurs in the hydrostatic column if pressure at point 0, where it is least, is equal to that of vapors of the liquid, practically zero. In this model the condition of a break is

$$P_0 = \frac{\omega^2 d_1}{6g_0}(h_1^2 - h_1 h_2 + h_2^2) = 0. \tag{18}$$

An analogous calculation for Clark's model gives

$$P_0 - \frac{\omega^2 d_1}{2g_0}\left(\frac{E_1}{E_1 + E_2}\,h_1^2 + \frac{E_1}{E_1 + E_2}\,h_2^2\right) = 0. \tag{19}$$

Under actual conditions $h_1$ is close to $h_2$ and $E_1$ is close to $E_2$ (most probably rotation around the center of inertia of a living object). With $h_1 = h_2$ from (18) and (19) it follows:

$$P_0 - \frac{\omega^2 d_1}{6g_0}\,h_1^2 = 0 \tag{18a}$$

and

$$P_0 - \frac{\omega^2 d_1}{2g_0}\,h_2^2 = 0. \tag{19a}$$

If we consider (18a) and (19a) as equations for $\omega$, then formally the first equation gives a value of $\omega$ which is $\sqrt{3}$ times greater than the second. In Clark's model, $h$ is the distance between centers of elastic volumes, equal to approximately half the length of the modeled object, so that from the second equation we obtain a value of $\omega$ which is 1.2 times greater than the first. Let us estimate what angular speed $\omega_p$ must be in order for a break to occur in the

hydrostatic column. Let $P_0$ be one atmosphere, $h_1 = h_2$ be on the order of three fourths of a meter, density of the liquid close to that of water. Based on formula (18a), we obtain $\omega \approx 32$ rad/sec $\approx 5$ revolutions per second. This result should actually imply "not less than 5 revolutions per second," as the pressure of tissues on the vessel was not taken into account.

Now let us try to find out how the above models correspond to actual physiological systems. The effect developing with acceleration can be divided /105 into: 1) initial mechanical and 2) strictly physiological. Let us assume that point (1) meets no objections from physiologists because even in the very earliest periods after the start of the force there are special physiological reactions to acceleration in the body. It is evident that these diverse reactions with different latent periods appear only after initial mechanical shifts reach certain threshold levels. In particular, about 7-10 seconds elapse before the onset of vasomotor compensation can be ascertained. Thus, for at least 5-6 seconds changes in pressure occurring in the vascular system under the influence of acceleration are determined only by running mechanical properties of the system. The above brief analysis of physical conditions of accelerations applies both to initial hydrostatic shifts and (primarily) to the tendency of pressure distribution which is maintained throughout the entire exposure period and which physiological compensation attempts to overcome.

Pressure distribution in the vascular system during acceleration is a function of another series of factors which we have not yet discussed, connected both with the vascular system itself and extravascular in origin. Among the latter an especially important role is played by pressures in the chest and abdominal cavities. The role of these factors will not be discussed here. We shall limit ourselves to considering only some additional parameters related to hemodynamics which take part in the formation of the distribution curve during acceleration. In a closed static system (in the absence of circulation), of course, there can be no other distribution but linear or parabolic. In vessels there are gradients connected with the dynamic component of pressure. Hydrostatic and dynamic pressures are additive values and according to the equation of total energy of the blood are summed:

$$P_0 = \rho g h + P + \frac{1}{2}\rho v^2, \qquad (20)$$

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where $P_0$ is the total thrust of the blood in pressure units, $\rho gh$ is hydrostatic pressure, $\rho$ is the density of the blood, P is the pressure of the blood, $\frac{1}{2} \rho \nu^2$ is kinetic energy per unit volume (it has the dimension of pressure). P is blood pressure recorded with lateral (perpendicular to the axis of flow) connection of a manometer to a horizontal vessel. As is known, under these conditions the first and third terms of the equation do not participate in formation of the recorded value. The meaning of P is found by determining the /106 difference between pressures at two points of the vessel which are h distance apart under the above measurement conditions. Then:

$$\Delta P_0 = \frac{8Q\mu h}{\pi r^4} = \Delta P ,$$ (21)

where Q is flow rate, $\mu$ is the viscosity of the blood, r is the radius of the vessel. Gradient $\Delta P$, therefore, is the pressure drop in a certain section of the vessel because of resistance loss. Below we shall designate this as $\Delta P_{dyn}$*.

For main arteries and veins, forming the largest part (in length) of the hydrostatic column h, the total gradient of $\Delta P_{dyn}$ is extremely low.

The greater part of pressure drop $\Delta P_{dyn}$ occurs in a small percentage of h at the ends of the hydrostatic column, while in the remaining part $\Delta P_{dyn}$ does not exceed 10-20 mm Hg. At the same time the hydrostatic pressure drop with h = 0.4 and +6.34 $g_z$ acceleration reaches, as the above calculation shows, almost 180 mm Hg. The presence of initial dynamic gradients of $\Delta P_{dyn}$ (in a horizontal vascular channel, with "lateral" measurement) cannot essentially alter the shape of the total pressure distribution curve during accelerations as compared with the curve for a static system. But because of changes in the caliber of vessels in the case of vasomotor compensation pressure drop $\Delta P_{dyn}$ in some sections can be altered, as a result of which the slope of corresponding parts of the total distribution curve $P_0(h)$ will also be changed.

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*The second term of Equation (20), P, in view of historically honored tradition, designates simply "blood pressure" or "static pressure" [1], although to distinguish it from the first term of the equation it would be more correct to call it "dynamic pressure." The latter name is conferred on the third term of Equation (20), which in a physical sense should be called "kinetic pressure."

It is interesting that G. I. Mchedlishvili [5] describes a completely |
closed common carotid artery as the result of active vasoconstriction. This
indicates the possibility that the discrepancy (observed in experiments) be-
tween empirical and theoretical data can be explained by reactive vasoconstric-
tion in the "lower" part of the hydrostatic column.

In conclusion, several words about the actual existence of a hydro-
statically indifferent point. It is evident that in view of changes in the
location of the HIP, depending on the tone of various sections of the vascular
system, it is appropriate to indicate the probability of placing a point with
the indicated properties in a certain area.

## REFERENCES

1.   Bayer, K.  Biofizika (Biophysics).  Moscow.  "Mir.", 1966.          /107

2.   Klimovitskiy, V.Ya.  In the book:  "Vliyaniye ioniziruyushchikh izlucheniy
     i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy"
     (The Effect of Ionizing Radiations and Dynamic Factors on Functions of
     the Central Nervous System).  Moscow, "Nauka", 1964, p. 33.

3.   Klimovitskiy, V.Ya.  In the book:  "Vliyaniye faktorov kosmicheskogo poleta
     na funktsii tsentral'noy nervoy sistemy" (The Effect of Space Flight
     Factors on Functions of the Central Nervous System).  Moscow, "Nauka",
     1966, p. 11.

4.   Klimovitskiy, V.Ya., N.N. Livshits and I.M. Rodionov.  In the book:  "Neko-
     torye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space
     Neurophysiology).  Moscow, "Nauka", 1967, p. 57.

5.   Mchedlishvili, G.I.  Funktsii sosudistykh mekhanizmov golognogo mozga
     (Functions of Vascular Mechanisms of the Brain).  Leningrad, "Nauka",
     1968.

6.   Pashutin, V.V.  Lektsii obshchey patologii (Lectures on General Pathology).
     St. Petersburg, 1881.

7.   Savin, B.M.  Gipervesomost' i funktsii tsen-ral'noy nervnoy sistemy
     (Gravitational Overloading and Functions of the Central Nervous System).
     Leningrad, "Nauka", 1970.

8.   Britton, S.W.  Amer. J. Physiol., Vol. 156, No. 1, 1949, p. 1.

9.   Clark, J.H., D.K. Hooker and L.H. Weed.  Amer. J. Physiol., No. 109,
     1934, p. 166.

10.  Duomarko, J. and R. Rimini. Congress de Cardiol., 4. Paris, 1950.
     Cited in: Gravitational Stress in Aerospace Medicine. London, 1961.

11.  Gauer, O.H. In: Gravitational Stress in Aerospace Medicine. London,
     1961, p. 257.

12.  Gauer, O.H. In: Gravitational Stress in Aerospace Medicine. London,
     1961, p. 16.

13.  Gauer, O.H. and E.A. Gienapp. Science, No. 112, 1950, p. 404.

14.  Gauer, O.H. and J.P. Henry. Aerospace med., Vol. 35, No. 6, 1964, p. 533.

15.  Gauer, O.H. and W.E. Hull. Feder. proceed., No. 1, 1954, p. 52.

16.  Lawton, R.W. In: Gravitational Stress in Aerospace Medicine. London,
     1961, p. 28.

17.  Lindberg, E.F. and E.H. Wood. In: Physiology of Man in Space. London,
     1963, p. 61.

18.  MacDonald, W.S. Blood Flow in Arteries. London, 1964.

19.  Salzman, E.W. and S.D. Leverett. Circul. Res., No. 4, 1956, p. 540.

20.  Sicker, O. In: Gravitational Stress in Aerospace Medicine. London,
     1961, p. 53.

21.  Wood, E.H., E.H. Lambert, E.J. Baldes and C.F. Code. Feder. Proceed.,
     No. 5, 1946, p. 327.

22.  Wilkins, R.W., S.E. Bradley and S.K. Fridland. Clin. Invest., No. 29,
     1950, p. 940.

# COMPARATIVE STUDY OF
## OXIDIZING METABOLISM OF NERVE TISSUE
## WITH VIBRATION STIMULATION IN VIVO AND IN VITRO

### L. D. Luk'yanova, L. M. Murashko

Previously we showed the existence of phase changes in oxidizing metabolism in the central nervous system during and after vibration stimulation of animals. During brief vibration (75 cps, 0.4 mm, 15 min.) the consumption of oxygen by brain tissues is increased and oxygen pressure reduced. It is accompanied by generalized excitation encompassing the central nervous system. The post-vibration period is characterized by reduced oxygen utilization in the cerebral cortex and a number of subcortical formations. Comparison of these data with changes in electric activity in the brain, as well as cerebral volume circulation and temperature [5-9], showed that changes in metabolism are the initial shifts in the development of subsequent changes also connected with a stable focus of excitation in higher sections of the central nervous system developing in the first phase. These studies and conditioned reflex experiments indicate a state of generalized inhibition in the post-vibration period, suggesting pronounced weakening of the stimulating process of the nervous system.

Changes can also be observed in respiratory metabolism of other tissues which are connected with vibration stimulation. Nevertheless, only in the nervous system are they expressed so positively and clearly.

Vibration sensitivity is controlled by central mechanisms. However, the direct mechanical effect of vibration on cells of various tissues is known. Denny-Brown and Brenner [17] showed that a single vibration causes direct injury to myelin sheaths of isolated nerves and segments at the place where myelin changes to endoneurium.

A. Ye. Shcherbak [16], studying the effect of local vibration, also noted hemorrhages in the spinal cord. Degenerative changes after a single vibration were noted in gray and white matter of the spinal cord and the brain by Ye. Ts. Andreyeva-Galanina and V. G. Artamonova [1].

According to the data of L. Ch. Minetskiy [13], longer contact with vibration causes hemorrhages and accumulations of blood in the spinal cord, disturbances of

mineral metabolism in bones and structural disturbances in the bones and spine.

N. K. Karpova [2], after 47-day local vibration of the paw of a rabbit, observed morphological changes in various sections of its nervous system. There were degenerative changes in axons and myelin sheaths of nerves and swelling and vacuolization of cytoplasm in Schwann's cells; decay of individual bundles of    /109 nerve fibers was noted, sometimes their regeneration  and decay of myelin in centers connected with the intact extremity. There were no dystrophic changes in nerve cells. Reactive changes were found in cells of the anterior, lateral and posterior horns of gray matter in the spinal cord. Vascular dilation was observed in the spinal cord and sheaths, hyperemia, hemorrhages in white matter and demyelinization in roots of the spinal cord.

On the other hand, D. N. Nasonov and B. S. Ravdonik [14] showed a paranecrotic reaction in protoplasm of muscle fibers and nerve cells of spinal ganglia after mechanical vibrations of sonic frequency. This reaction is general and unidirectional for many tissues of the body both in vivo and in vitro [3, 15]. I. Shevts and N. G. Kuz'mina found pronounced shifts in protoplasm in cells under the effect of vibration. These shifts consisted of increased sorption properties of the cell and its intense diffuse color instead of granularity. This process corresponds, according to D. N. Nasonov, to a paranecrotic state of the cell.

Thus, initial disturbances in living cells can be mechanical as well as biochemical changes, depending on the strength of stimulation, and similar, evidently, to thixotropy of colloids.

However, in studying the reaction of the entire organism, taking into account the neurohumoral effect on the course of various processes, we must not fail to consider the possibility of a reflex effect of vibration on the development of initial processes. According to the data of I. Shevts and N. G. Kuz'mina [15], actuation of the function of the brain or spinal cord caused symptoms of paranecrosis to disappear or be much less pronounced than in normal animals.

The purpose of this work was to study initial mechanisms controlling and regulating energy metabolism in nerve tissue during vibration stimulation of the entire organism and the direct effect on isolated nerve tissue.

## Methods of study

Studies were made on white male rats. Subjected to vibration (70 cps, 0.4 mm, 15 min.) were both the animals themselves and slices of cerebral cortex at various lengths of time after their extirpation. The animals were exposed to 5 and 15 minute single vibrations. After various intervals (from 5 to 30 min.) the rats were killed and slices of cerebral cortex removed to study respiratory metabolism. In addition we also studied the effect of multiple vibration on the oxidizing metabolism of nerve tissue. In this case the rats were exposed to daily 15 minute vibration. Brain tissue was extirpated for study of respiratory metabolism 15-30 minutes after the second, third and tenth vibration.    /110

In the second part of the study, slices of cerebral cortex of intact animals were placed in a glucose-saline solution and exposed to vibration. Conditions of vibration were the same as above. After various intervals of time after vibration we tested the respiratory metabolism of the slices.

Respiration and the state of the respiratory chain (study of gradations of metabolic states) were determined by polarography. To study slices of tissue a special polarographic unit was developed, making it possible to maintain the integrity of the slice during polarographic measurements and thermostatic control of the reaction medium. Oxygen consumption was determined by ordinary polarography by the gradient of the drop in limiting diffuse current (V = 0.65v), reflecting change in the concentration of oxygen dissolved in the unit as the result of its utilization by the slices. The measuring unit was made of a stationary platinum electrode covered with an oxygen-selective film (teflon 5µ) and an indifferent electrode (AgCl)(Fig. 1). Uniform mixing of the reaction medium was provided by a magnetic mixer. The design of the unit provided for the possibility    /111 of introducing various kinds of additions.

Respiratory metabolism and the reactivity of cerebral cortex slices were evaluated by measuring metabolic states according to the method of Chance. For this, respiratory activity of tissue was measured in a saline solution (pH = 7.4, t = 37°) without exogenous substrates of oxidation: in the presence of succinate and with the addition of ADP. This sequence, on one hand, made it possible to evaluate the 3rd (active) and 4th (control) metabolic states, to determine respiratory control, phosphorylation rate and the behavior of tissue in an impoverished
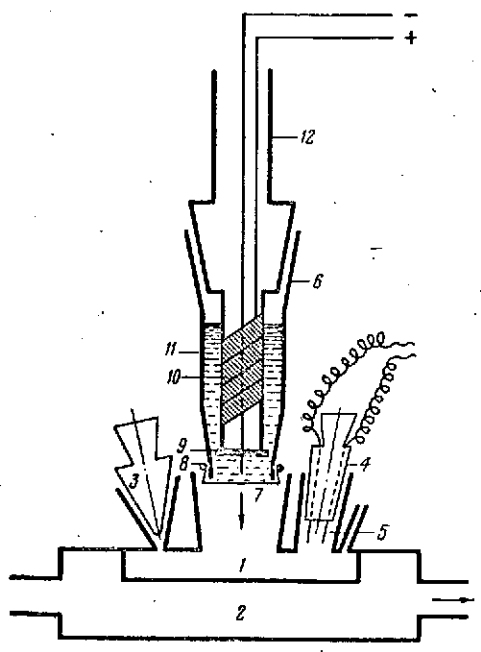
Figure 1. Diagram of the polarographic unit and "oxygen cathode".

1 — unit for measuring respiration; 2 — thermostating chamber; 3 — cork covering the opening for adding various substances into the unit; 4 — cork covering the opening through which tissue is placed into the unit; 5 — platinum tissue supports; 6 — case of the measuring unit; 7 — teflon film; 8 — rubber ring for holding the film; 9 — platinum electrode (cathode); 10 — silver chloride electrode (anode); 11 — electrolyte; 12 — electrode support.

medium (additional functional test) and to conduct a general comparative analysis of gradations of metabolic states. On the whole, everything created a detailed picture of the state of the respiratory chain in test tissue. In some cases respiratory activity of slices of the cerebral cortex was measured in a glucose-saline solution.

## RESULTS OF STUDIES
### The effect of a single vibration in vivo

We found the following regularities in studying the respiratory activity of cerebral cortex slices from animals exposed to preliminary vibration of various length.

The intensity of respiration in slices of the cerebral cortex and the caudate nucleus, obtained after 5-minute vibration stimulation of the animals, significantly exceeded control levels if the reaction medium contained glucose as a substrate of oxidation. In the case of 15-minute vibration of the animals, respiration of slices was inhibited in this medium (Table 1). However, in a medium deprived of exogenous substrates, in the case of 15-minute single vibrations, as with briefer stimulation, there was not a reduction but an intensification of respiration (Table 2).

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Table 1

CHANGE IN RESPIRATION OF SLICES OF CEREBRAL CORTEX AND CAUDATE
NUCLEUS IN A GLUCOSE-SALINE MEDIUM AFTER VIBRATION OF THE ANIMALS

| Group | Oxygen consumption, mμA/mg/min | | | |
|-------|-------------------|-------------------|-------------------|-------------------|
| | 5-minute vibration | | 15-minute vibration | |
| | cerebral cortex | caudate nucleus | cerebral cortex | caudate nucleus |
| Test Control | 2.92±0.2 2.15±0.12 p<0.01 | 2.35±0.13 1.81±0.09 p<0.05 | 1.50±0.07 2.15±0.12 p<0.01 | 1.24±0.06 1.81±0.09 p<0.01 |

Table 2

CHANGES IN RESPIRATION OF SLICES OF CEREBRAL CORTEX AND CAUDATE
NUCLEUS IN  A MEDIUM WITHOUT EXOGENOUS SUBSTRATES
AFTER VIBRATION OF THE ANIMALS

| Group | Oxygen consumption in mμA/mg/min | | | |
|-------|-------------------|-------------------|-------------------|-------------------|
| | 5-minute vibration | | 15-minute vibration | |
| | cerebral cortex | caudate nucleus | cerebral cortex | caudate nucleus |
| Test Control | 2.42±0.13 1.88±0.09 p<0.01 | 2.10±0.10 1.65±0.08 p<0.01 | 2.85±0.14 1.88±0.09 p<0.01 | 1.98±0.10 1.65±0.08 p<0.05 |

These data force a return to more detailed study of the change in metabolic
states of tissues from animals exposed to vibration.  In these tests succinate was
used as a substrate of oxidation (Fig. 2).

From Fig. 2 it follows that the differences in respiratory reaction to the
addition of succinate and ADP between animals which have been exposed only to the
sound of the vibrostand or to vibration are insignificant.  In both cases res-
piration is inhibited.  In the presence of succinate and ADP, with only the
noise, it is even more pronounced.
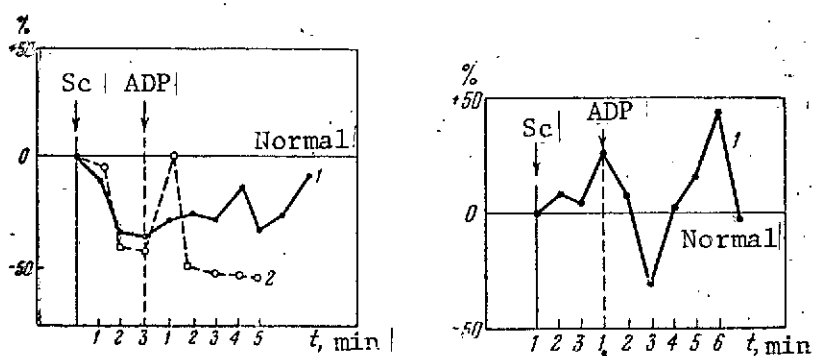
Figure 2. Change in respiratory reaction of cerebral cortex tissue of rats exposed to vibration (15 minutes).

Sc — addition of succinate (1 x $10^{-2}$ M)(changes shown in % of first 5 min.);

ADP — addition of ADP (2 x $10^{-2}$ M)(changes in % of respiration before addition of Sc);

1 — vibration; 2 — listening to noise of the vibrostand
All values correlated with the control group of animals (normal), not exposed to vibration.

Figure 3. Change in metabolic reaction of cerebral cortex tissue of rats exposed to 5-minute vibration.

Symbols same as in Fig. 2.

In the group of vibrated animals cases when succinate had only an inhibiting /11: effect on respiration increased markedly.

Not only single vibrations, therefore, but also listening to the noise of the vibrostand has a perfectly clear effect on the respiration of nerve tissue.

Different relationships are observed in cases when vibration is briefer and, as was shown previously, in the central nervous system there is only time for the stage of excitation to develop, not proceeding to subsequent inhibition (5-minute vibration). Endogenous respiration of cerebral cortex slices and their respiration with succinate is increased (Fig. 3). However, the quantitative ratio between positive and negative reactions to succinate remains constant. The metabolic response to the addition of ADP, as in the case of 15-minute vibration, reveals a tendency toward increased negative reactions (inhibiting effect). Nevertheless, on the whole the stimulating effect of both succinate and ADP increases in comparison with the control.

## The effect of multiple vibration
## on oxidizing metabolism of nerve tissue

With multiple forces of vibration on animals the successive development of typical changes in oxidizing metabolism of nerve tissue was observed during the first 10 applications of this stimulus (Figs. 4-5). Brain tissue of rats was removed 15-30 minutes after 15-minute vibration. Curves in these illustrations take into account the difference between the control and test groups of animals. We must note that the intensity of tissue respiration in the brain progressively dropped as the total number of vibrations increased ("accumulation" of vibration). Against this background a phase change is observed in the respiratory reaction to the addition of succinate and ADP. In both the cerebral cortex and the caudate nucleus a period of distinct increase in their inhibiting effect on respiration is recorded (1-2nd day), relative normalization of the metabolic reaction (3rd day) and its secondary disturbance in the same direction as in the first period (10th day)(see Figs. 4-5).

Changes in these metabolic indices are the result of values for all tested cases, obtained by summarizing variously-directed responses whose ratio changes during the forces. After several initial vibrations there are a number of reactions in which the inhibiting effect of succinate on respiration is seen.



Days, number of vibrations



Days, number of vibrations
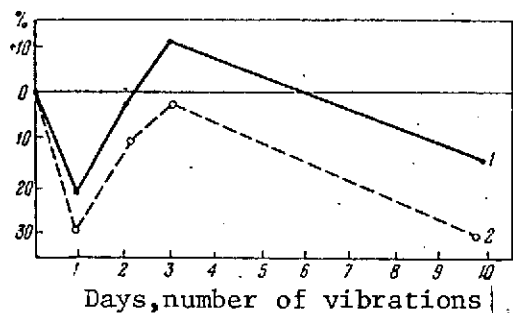
Figure 4. Change in respiratory reaction of cerebral cortex tissue of rats exposed to multiple daily 15-minute vibration.

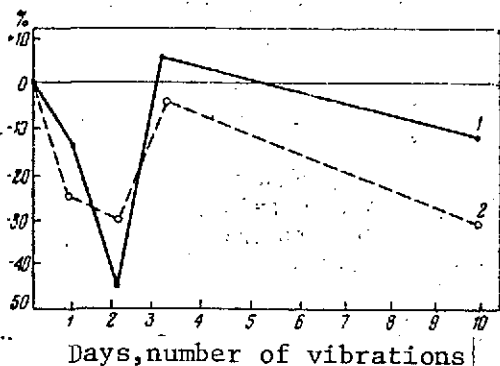1 — change in reaction to Sc (in % of control); 2 — same to ADP (in % of control).

Figure 5. Changes in respiratory reaction of nerve tissue obtained from subcortical sections of rats exposed to multiple daily 15-minute vibration.

For symbols see Fig. 4.

However, later their proportion decreased slightly, although still significantly exceeding normal. Just as under the influence of vibration, the number of reactions in which the inhibiting effect is evident with the addition of ADP increases in comparison with intact animals. Unlike the preceding |case, it increases during multiple vibration.

## The effect of vibration on slices of cerebral cortex

Previously we showed [10-12] that isolated slices of cerebral cortex are distinguished by their functional characteristics at different periods after extirpation. It is natural to expect that if vibration has any effect on isolated nerve tissue it will depend on the period of the test.

In fact, when isolated nerve tissue is vibrated the following regularity became evident, depending on the age of the slices. 15-minute vibration of relatively fresh slices (first 30 minutes after their removal) led to an increase in the number of cases in which there was initial inhibition of respiration with the addition of succinate, while its later stimulating effect was slightly
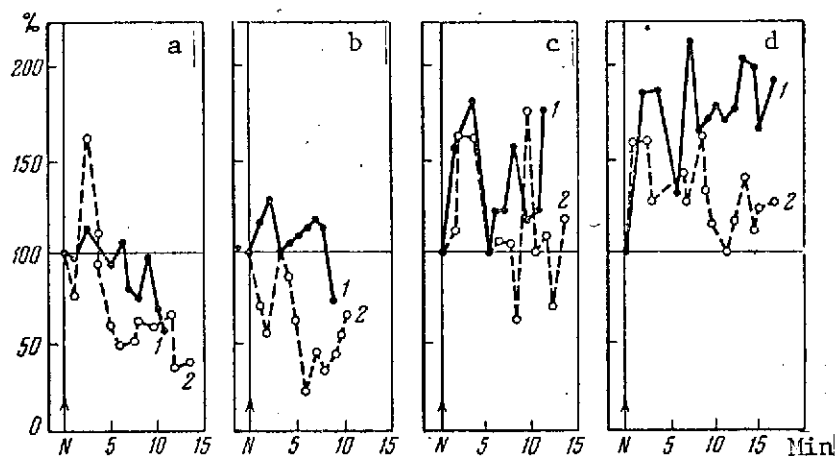
Figure 6. Changes in respiratory reaction of cerebral cortex slices exposed to 15-minute vibration. |

1 — reaction to the addition of succinate (in % of endogenous respiration);
2 — reaction to the addition of ADP (in % of respiration in the presence of Sc);
a — slice after 30 min.; b — slice after 1 hour; c — slice after 2 hours;
d — slice after 4 hours.

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greater than for control slices. In response to the addition of ADP there
was a predominance of cases in which the inhibiting effect of the phosphate
acceptor appeared. However, where it was stimulating, it was more pronounced
with a well-marked transition from 3 to 4 stages (Fig. 6, a). 15-minute vi-
bration of older slices increased the number of cases in which only the stimu-
lating effect of succinate on respiration appeared (Fig. 6, b-c). However, the
degree of this effect was slightly weaker than in the control. A different
picture was seen with the effect of ADP. Vibration of slices an hour after
extirpation of the tissue caused the number of cases in which the inhibiting
effect of ADP appeared to remain as high as earlier. However, the degree of
repression of respiration was stronger (see Fig. 6, b).

This effect disappeared after 2 hours and all the more after 4 hours.
In the latter case the number of reactions in which the addition of ADP
stimulated respiration was even slightly higher than in the control. In addi-
tion the effectiveness of ADP was clearly increased. Phosphorylation time was
reduced (2.6±0.12 min. against 6.3±0.42 min. in the control). In the majority of
cases there was pronounced respiratory control, greater than in the control
(2.56±0.28 against 1.92±0.2 min.).

Vibration stimulation, therefore, affects the direction of metabolic      /116
processes taking part in the response. This is indicated not only by the above
noted changes, but also by changes in endogenous respiration. Thus, in the first
30-35 minutes vibration of slices (15 minutes) caused inhibition of endogenous
respiration (1.02±0.05 mμA O/mg/min. instead of 1.20±0.065 mμA O/mg/min.).
Changes in metabolic reactivity observed after vibration of the slices were main-
tained for a long time. Similar changes to those described above were observed
even 30 minutes after stimulation ended.

Obvious changes are, therefore, present in the energy metabolism of the
nerve cell under the influence of vibration. However, in the process of isolating
nerve tissue vibration sensitivity of the cell changes, leading eventually to a
qualitatively different expression of the results.

## Discussion of results

On the basis of our earlier tests in vivo, it was shown that vibration causes phase changes in oxidizing metabolism in brain tissue [5]. Because of methodological difficulties preventing completely accurate differentiation of the start of metabolic shifts and the effect on them of blood flow in an intact organism, it became necessary to conduct more direct tests which could help to reveal the true nature of these phase changes.

Series of tests studying metabolic changes in isolated brain tissue developing under the effect of vibration of animals in situ should help answer the question: are these phase changes, recorded in vivo by the change in "oxygen load," really determined by disturbances in the work of the respiratory chain.

Increased respiratory activity of brain slices in a glucose-saline medium after 5-minute vibration of the animals and its reduction after 15-minute vibration indicate that analogous changes observed in the "oxygen load" in vivo are the result of corresponding changes in respiratory metabolism in nerve tissue. Therefore, vibration with the parameters used in this work actually increases the rate of oxygen consumption in the first few minutes, but more prolonged action has the opposite effect. Metabolic changes developing then are maintained after death of the animals and are reproduced in slices of medullary tissue from various sections of the central nervous system.

A slightly different response when succinate is used as the reaction medium for the slices and in the absence of exogenous substrates does not contradict the above. In the intact organism the main substrate of oxidation is glucose and with its utilization the effect is the same in vitro and in situ. With the use of other substrates or in their absence the recorded changes can be connected with the specificity of metabolic paths realized here, leading to a different outward effect.

Analysis of metabolic states under the effect of exogenous succinate shows that with a single application of a 15-minute vibration stimulus the inhibiting effect on respiration of both succinate and ADP is increased. In the case of freshly-isolated slices we connected this effect with the specific state of "post-hypoxic activation" when the usual course of substrate oxidation in the tricarboxylic acid cycle is disturbed and respiration proceeds by switching to the oxidation of endogenous succinic acid [4, 10]. Here the exogenous substrate

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either stops stimulating respiration (excess formation of endogenous succinate) or can even inhibit respiration ("conjugating" effect of substrate). Evidently the latter will occur when a balance is established between the amount of endogenous succinate formed (it does not exist in excess) and the rate of its oxidation. If this is so, then increase in the inhibiting action of the exogenous succinate should reflect the increased consumption of endogenous succinate, i.e. even greater activation of this path of oxidation under the influence of vibration. However, such a state is possible only after the application of a vibration stimulus of sufficient length (15 minutes). In the case of 5-minute vibration an increase in the stimulating effect of succinate was noted which can be connected with the disturbed balance between the intake and consumption of endogenous succinate because of the excess of the latter over the former. This possibility is also suggested by increase without such high endogenous respiration as well as the low effectiveness of ADP, which at this period is connected not with oxalic-acetic inhibition of respiration but with the presence of a high concentration of free acceptors of phosphate in tissue samples. Therefore, the increase in the inhibiting effect of succinate with 15-minute vibration of the animals is secondary, reflecting phase changes during and immediately after vibration stimulation which we found in studying the oxidizing metabolism of the brain in chronic tests on the entire animal.

Metabolic changes found with the multiple application of vibration also verify our earlier conclusions about the complex, variable reaction of the organism in response to regular application of this stimulus.

The sharpest disturbances are observed after the first-second application of vibration. Then follows a weakening of the effect of vibration (3rd day) and its secondary increase. We obtained an analogous direction of changes in studying respiration of the brain in vivo.

Comparison of the results obtained in vibration stimulation of animals and isolated slices of cerebral cortex reveal the basic similarity of changes in the respiratory metabolism of nerve tissue in both cases, indicating the generality of the mechanisms regulating intracellular energy metabolism.

With vibration of isolated nerve tissue in vitro variants of responses obtained in vivo are maintained. They depend, however, on the functional state of nerve tissue and its energy regulation.

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With 15-minute vibration of freshly-isolated tissue samples (first 30 minutes after their extirpation) the observed metabolic changes are somewhat in the middle between the effect of 5 and 15 minute vibration in vivo. Endogenous respiration of slices was reduced, however, the effectiveness of the stimulating effect of succinate was increased, which can be evaluated, in connection with the above reasons, as the activating action of stimulation on oxidizing processes in isolated tissue. However, the effect of vibration on nerve tissue in situ is strengthened and is accompanied by more pronounced changes in oxidizing metabolism.

This is also understood. Vibration stimulation of the entire organism has a direct effect on numerous receptors; for several it is adequate. The direct effect of this kind of stimulus on vestibular, auditory, motor and skin analysors can also be indicated with rather high certainty. Vibration stimulation, therefore, is summarized in the central nervous system because of the arrival of signals along many channels from many receptors. The development of stagnant centers of excitation is completely possible, both in the spinal cord and in higher sections of the central nervous system as the result of overstimulation of nerve cells.

Isolated nerve tissue is limited in its possibilities of receiving such extensive exciting information with stimulation as its connection with afferent pathways of stimulating impulses is disturbed. This is the first factor reducing the effect of vibration in vitro. However, to this are also added the changes in the functional state of nerve cells resulting from their removal from the body, which of itself is a stress stimulus. Metabolic sensitivity of such tissue also changes during the process of aging.

An hour after extirpation of the tissue, 15-minute vibration causes, as already pointed out, a predominance of metabolic responses in which the inhibiting effect of ADP is pronounced. However, it has a completely different meaning in case of freshly-isolated slices. By this time metabolic ratios in tissue specimens are established which are typical of the area of energy regulation with restoration of the normal Krebs cycle [10]. In this case, the inhibiting effect of ADP on respiration also indicates weakening of energy regulation under the influence of vibration stimulation resulting in oxalic-acetic inhibition of respiration (specific for this state) [4]. Thus, vibration of slices during this

period causes a transition to the area of low-energy regulation, i.e. to weakening of the effectiveness of the tissue respiration chain.

At a still later period vibration stimulation not only outwardly does not disturb respiration of the slices, but also seems to increase the work of the respiratory chain (see Fig. 6, c, d). This is more evident the older the slice, i.e. the greater the shift to the area of low-energy regulation before vibration. This all gives basis for feeling that the improvement after vibration is "imaginary." It can be connected with weakened reactivity and loss of sensitivity of isolated nerve tissue to external stimuli during the aging process of the tissue [10]. A stress stimulus, which under all other conditions would lead to sharp disturbances, at this moment can, evidently, only insignificantly activate work of the respiratory chain without symptoms of overstimulation.

Nevertheless, the presence of a direct effect of vibration on isolated nerve tissue must be acknowledged, causing corresponding changes in its energy metabolism in the nerve cell.

## Conclusions

1. Single 5-minute vibration of rats (70 cps, 0.4 mm) increases respiration of brain tissue, while 15-minute depresses it. These changes are accompanied by specific changes in energy metabolism in nerve tissue.

2. Phase changes in respiration, observed with single and multiple application of vibration stimulation using an "oxygen" electrode in vivo, is actually connected with corresponding changes in oxidizing metabolism of brain tissue.

3. Vibration stimulation can have a direct effect on oxidizing metabolism of the nerve cell. The direction of this effect changes during the process of isolating nerve tissue and is determined by the level of energy regulation of tissue during the test period.

## REFERENCES

1. Andreyeva-Galanina, Ye.Ts. and V.G. Artamonova. Ekspertiza trudosposob-  /120
      nosti pri vibratsionnoy bolezni (Expert Examination of Work Ability
      During Vibration Sickness). Leningrad, Medgiz., 1963.

2. Karpova, N.I. Trudy Leningr. sanitarno-gigien. med. in-ta., No. 75,
      1963, p. 20.

3.  Kondrat'yeva, T.M.  Arkhiv biol. nauk., No. 5, 1934.

4.  Kondrashova, M.N.  In the book:  "Mitokhondrii" (Mitochondria).  Moscow, "Nauka", 1971.

5.  Luk'yanova, L.D.  In the book:  "Vliyaniye ioniziruyushchikh izlucheniy i dinamicheskikh faktorov na TsNS" (The Effect of Ionizing Radiations and Dynamic Factors on the Central Nervous System).  Moscow, Izd-vo AN SSSR, 1964, p. 128.

6.  Luk'yanova, L.D. and S.M. Ambrosova.  In the book:  "Vliyaniye faktorov kosmicheskogo poleta na funktsii TsNS" (The Effect of Space Flight Factors on Functions of the Central Nervous System).  Moscow, "Nauka", 1966, p. 95.

7.  Luk'yanova, L.D. and Ye.P. Kazanskaya.  Ibid., p. 81.

8.  Luk'yanova, L.D., A.V. Kol'tsova, Ye.S. Meyzerov and Ye.P. Kazanskaya.  Ibid., p. 105.

9.  Luk'yanova, L.D. and V.Ya. Klimovitskiy.  In the book:  "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space Neuro-physiology).  Moscow, "Nauka", 1967, p. 145.

10.  Luk'yanova, L.D.  Okislitel'nyy metabolizm i reaktivnost' nervnoy tkani v perezhivayushchikh preparatokh v usloviyakh tselostnogo organizma (Oxidizing Metabolism and Reactivity of Nerve Tissue in Isolated Specimens Under Conditions of the Entire Organism).  Doctoral dissertation.  Moscow, 1971.

11.  Luk'yanova, L.D., L.G. Khaspekov and L.M. Papulova.  Biofizika., Vol. 5, No. 16, 1971, p. 872.

12.  Luk'yanova, L.D. and V.Ye. Shungskaya.  Trudy Ivanovskoy konferentsii po biokhimii dykhaniya, No. 1, 1970, pp. 43 - 49.

13.  Minetskiy, L.Ch.  Trudy Leningr. sanitarno-gigien. med. in-ta., No. 61, 1960, p. 16.

14.  Nasonov, D.N. and K.S. Ravdonik.  Fiziol. zhurn. SSSR., Vol. 5, No. 33, 1947, p. 569.

15.  Shevts, I. and N.G. Kuz'mina.  Gigiena i sanitariya., No. 9, 1956, p. 37.

16.  Shcherbak, A.Ye.  Obozreniye psikhiatrii, nevrologii i eksperim. psikhologii, No. 8, 1903, p. 561.

17.  Denny-Brown, D. and C. Brenner.  Neurosurg. Psychiat., No. 7, 1944, p. 46.

THE EFFECT OF VIBRATION ON THE DEVELOPMENT AND
MAINTAINANCE OF MAZE LEARNING IN RATS

Ye. M. Skobeyev

In recent years a great deal of attention has been directed toward study
of the effect of vibration on higher nervous activity in man and animals.  In
scientific literature significant data on the effect of this factor on the cen-
tral nervous system have already been accumulated [1, 2, 11, 21].  Researchers
using the conditioned-reflex method have found that with vibration the dominant
symptom in animals is depression of conditioned reflexes, sometimes accompanied
by inhibition of differentiations.  This phenomenon was recorded in tests on
rats investigating conditioned motor food reflexes using the method of L. S.
Kotlyarevskiy [4, 5, 7] and in tests on dogs [4].

Inhibition of conditioned reflexes was expressed differently in animals
with different types of nervous activity.  In animals with a strong type it
appeared in reduction and lengthening of the latent period of the conditioned
reflex.  In animals with a weak type, complete lack of all developed conditioned
reflexes and partial absence of natural reflexes  was observed for 1-2 days.
Disturbances in power ratios are typical of vibration effects, indicating excess
inhibition.  In individual tests on rats a complete ultraparadoxical phase was
recorded [8].  In monkeys exposed to the force of vibrations (5-40 cps, 6.0 mm,
2 g) increase was noted in the number of errors in solving problems selecting
an unpaired object, lengthening of the latent period of reactions and weakening
of attention.  In brain structures of these animals rhythms with the same
frequency as vibration were recorded [22].

With repeated vibrations their effectiveness is reduced [13].  For example,
in dogs of the strong balanced type, local vibrations on sections of the body
at the start of the test increased the amplitude of motor conditioned reflexes
and lengthened the latent period and after-action; however, with repeated expo-
sures these symptoms became increasingly less pronounced and after 9 hours were
not observed at all [18].

Compensation-adaptational phenomena have been shown in tests [13].  Rats were
exposed to 30 daily vibrations (70 cps, 0.4 mm, 15 min.).  After the first ex-

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posures a sharp reduction was observed in positive conditioned reflexes. Hypersynchronized high-amplitude rhythm in the electroencephalogram was maintained for 30-60 sec. after vibration. It was replaced by a phase of desynchronization, after which a bursting kind of activity developed. Depression of oxidizing processes after the force also verified the presence of severe inhibition in brain structures. Later, despite a prolonged effect, conditioned-reflex activity of the rat began to improve and after 21 exposures was stabilized without reaching the initial level. No more reduction of oxidizing processes was observed after the force but depression of bioelectric activity was noted in background electroencephalograms. During the force the reaction of hypersynchronized high-amplitude rhythms was often absent. In the opinion of the authors, these phenomena, indicating reduced excitability of the cortex to spontaneous|peripheral pulses or blocking of the latter at the subcortical level, underly adaptation to vibration. Thus, studies performed by various methods indicate that vibration causes certain changes in functions of higher sections of the central nervous system.

Radiobiological studies revealed important discrepancies in the results of tests conducted by the conditioned-reflex method and studying the behavior of rats in a maze, giving basis for concluding that in maze learning compensation resources of the brain are more pronounced (see article of N. N. Livshits and Ye. S. Meyzerov in this collection). /122

There has been interest in a detailed study of the effect of vibration on maze learning to determine the possibility of using it to reveal changes in higher nervous activity.

## Material and method

The study was conducted on male "Wistar" rats weighing 320-350 g. In the test group were 8 rats;| in the control,|7. Selected for tests were animals with high food excitability, rapid adaptation to experimental conditions and rather easily developed maze learning. In selecting test groups (the work was conducted with simultaneous | study of radiation, vibration and a combined force), 32 out|of 186 rats were selected, which is 17% of the total number. The percentage of rejection in this case was equal to that in the formation of groups of rats for conditioned-reflex studies [10].

In the vivarium all the rats were kept under the same conditions (4-5 animals in each cage) and given an identical diet. For 24 hours before the test, food was taken from them with the exception of water, milk and carrots. In the maze, rats reaching the goals were given sunflower seeds to eat. Each rat completed 5 tests per day. A total of 20 tests were conducted before activation of the force.

In selecting the animals, taken into account were indices of the last 10 tests, as results of the first days of testing, as is known, are subject to the effect of many attendant factors, in particular, the rate of extinction of external inhibition.

In the study we used a slightly-altered version of Leshli's maze III [6] (see Fig. 1 in the article of N. N. Livshits and Ye. S. Meyzerov et al., in this collection). The maze was placed in a sound-proof room. The experimenter remained outside the room and watched the behavior of the rats through an observation window. The rate of crossing the maze and the latent period were recorded automatically with an electric unit. After the rat was placed in the start compartment the maze was covered with transparent plastic. The passage out of the start compartment to the maze corridor was cut off by a plate which was raised by means of a handle when the recording instruments were turned on.

The maze was made of solid-color material and evenly lighted. Some data on the maze: volume 81,000 cm$^3$, area 5400 cm$^2$, height 15 cm, length of large blind passage 20 cm, width of the correct passage and blind alley 10 cm, area /123 of the large blind alley 200 cm$^2$, length of the small blind alley 10 cm, area of the small blind alley 100 cm$^2$, area of the feeding and start compartments 200 cm$^2$ each, length of the correct passage 300 cm. There were a total of 6 corridors in the maze and 12 blind alleys (8 large and 4 small).

In comparing the rate of development of skills under our conditions with corresponding indices described by several researchers in the USA [20], no essential difference was found.

The forces started after the rats reached criterion I of "skill" according to Vudvorts [3] (three errorless runs in a row), attained by all our rats after 8-14 tests.

On the basis of indices of behavior before attaining criterion I the characteristics of the animals were compiled and they were distributed in such a

manner that each rat exposed to vibration would have a partner with similar indices in the control group [7, 8, 9, 10].

Rats in the test group were exposed to vibration under the following conditions: frequency 70 cps, amplitude 0.4 mm, length of exposure 15 minutes. Operation of the vibrostand was accompanied by noise of 75 db. The rats in the control group were placed around the vibrostand but exposed to no vibration.

The force was produced three times: the interval between the 1st and 2nd exposures was 14 days, between the 2nd and 3rd 7 days; 21 days after the 3rd force maze learning was reversed. In this instance the feeding compartment became the start compartment for the rats and the start compartment the feeding area, the door was also correspondingly changed. Tests took into account: indices of the rate of attainment of second and third criteria of "skill" (5 and 10 errorless runs in a row, respectively) [3], as well as the speed of a maze run, latent period of the run (time between the opening of the exit to the maze and the start of the run) and the number of errors made (runs into blind alleys). The behavior of rats in the maze was studied immediately after the force, the next day and 24 hours later. A total of 3-4 tests per week were conducted. For statistical analysis of the data algorithm 31 was used to compare two regression series [17].

<div align="center">Results of the study</div>

Throughout the entire period of the tests, the rats in the control and test groups remained alert and active. During and after the forces the average weight of the rats in all groups also remained constant. Because it was difficult for us to establish a relation between the type of higher nervous activity and reaction to vibration because of the small number of animals and lack of    /124 specific examination of type, we feel it is more correct to speak not of typological but of individual differences. We found no reliable changes in the number of tests necessary to attain criteria II and III of "skill" in rats exposed to vibration. In both test and control groups criterion II was attained after 17-21 tests and the third after 30-32 tests.

For two weeks after the first force all indices of maze learning were rapidly improved in both the test and in the control groups under the influence of training. The latent period, time of maze run and the number of errors

sharply decreased.

In test rats the time of the maze run was slightly less than in the controls (Fig. 1), but the difference was not statistically reliable. In these same times rats exposed to vibration spent slightly more time after opening of the door in the start compartment. The difference in length of the latent period was also unreliable (Fig. 2). Test rats made fewer errors in crossing the maze than the controls during this time (Fig. 3). Differences between test and control groups according to this index were reliable by the criteria of difference of series and excess of one series over another (in both cases $p<0.01$).

After the second force, beginning with the 3rd week, the speed of the run in test and control groups was stabilized; control rats expended slightly less time than test animals, but the difference was insignificant. Beginning with the 4th week, in the test group an increase was noted in the latent period in comparison with the control and this difference was maintained until the end of the test, but was not reliable at any stage.

Differences between the number of errors (runs into a blind alley) in test and control groups became minimal in the 3rd week of observation and increased slightly later. Reliable superiority of test rats over controls according to this index was maintained at all stages.

A slight reduction in the average speed of a run was noted in the 6th week in control rats only because of rat No. 73, while in the other 6 control rats the speed of the run did not change significantly.

The increase in average latent period in control rats in the 3rd week is due to one rat (No. 24) increasing its time in the start compartment one day in comparison with the initial level; this was not typical of other rats in this group.

In conversion of learned skills no special difference was observed in the speed of runs between test and control rats; however, test rats took more time in the start compartment after the door was opened. After entering the maze test rats made fewer errors in attaining the goal.                    /125

In all these cases differences between test and control groups were not statistically reliable.
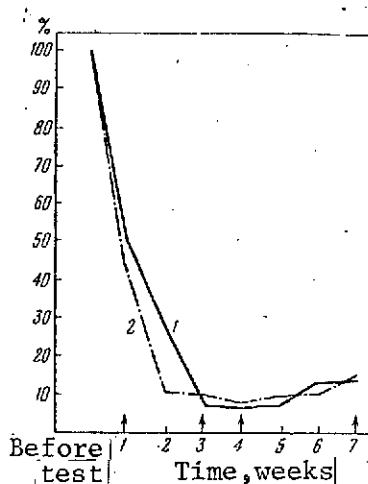
**Figure 1.** Average weekly time of run (in % of initial level).

Vertically — test index (in % of initial level, taken as 100%); arrows 1, 3, 4 — vibrations; arrows 7 — conversion of maze learning (II); 1 — control; 2 — rats exposed to vibration.
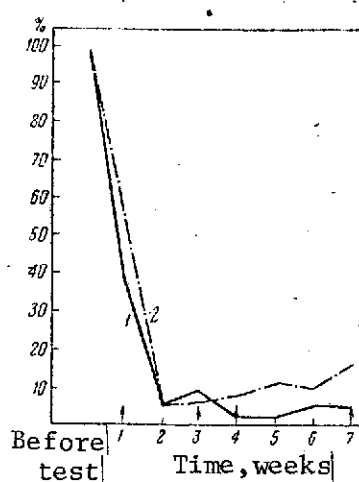
**Figure 2.** Average weekly time of latent period of exit into maze (in % of initial level).
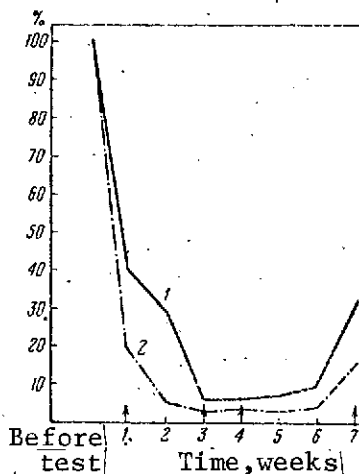
Symbols same as in Figure 1.



**Figure 3.** Average weekly number of errors (runs into blind alleys in % of initial level).

Symbols same as in Figure 1.

## Discussion

As noted in the introductory part of this article, a great deal of litera-
ture data verifies that vibration has a significant effect on the central nervous
system. In particular, in tests conducted by L. Luk'yanova et al., vibrations
with the same parameters as those we used caused clear cut changes in rat encepha- /126
lograms, two-phase changes in oxidizing processes in brain tissues and circulation

[12, 14].

After such forces we found no significant deterioration of behavior in rats in the maze. After the first force it is true an increase was observed in the latent period of the run, but the speed of the run during this time also increased. The latent period was stably lengthened after the third force, but its lengthening was not statistically reliable and the number of errors in all of these stages of observation in animals exposed to vibration was reliably lower than in the control group.

The results we obtained we explain not by lack of an unfavorable effect of the vibration which we used on functions of higher sections of the brain, but that the maze method evidently cannot always catch these effects.

I. P. Pavlov [16] indicated that in maze learning animals use information obtained simultaneously from several analysors which creates very favorable conditions for compensatory processes.

Reducing the number of errors in rats exposed to vibration can be considered a reaction of moderate stress, accompanied by hypercompensation.

Also not excluded is another interpretation. Vibration force in some dog tests caused increased conditioned reflexes with inhibition of differentiation [18]. It is possible that the maze method cannot reveal disturbances of the inhibition process if it is not sharply expressed, but a relative increase of some indices of higher nervous activity is easily caught by this method. This question requires special study.

## Conclusions

1. Vibrations with a frequency of 70 cps, amplitude of 0.4 mm for 15 minutes, applied three times with two and one week intervals, caused in rats a reliable reduction in the number of errors in crossing the maze.

2. It is verified that maze learning creates great possibilities for the compensation of disturbances caused by unfavorable factors.

3. It is assumed that the reduction in the number of errors in the maze, caused by vibration, is connected with the reaction of moderate stress, accompanied by hypercompensation.

REFERENCES

1. Andreyeva-Galanina, Ye.Ts., E.A. Drogichina and V.G. Artamonova. Vib-      /127
   ratsionnaya bolezn' (Vibration sickness). Leningrad, Medgiz., 1961.

2. Borshchevskiy, I.Ya., M.D. Yemel'yanov, A.A. Koreshkov, S.S. Markaryan,
   Yu.P. Petrov and V.G. Terent'yev. Obshchaya vibratsiya i yeyo vliyaniye
   na organizm cheloveka (General Vibration and Its Effect on the Human
   Body). Moscow, Medgiz., 1963.

3. Vudvorts, R. Eksperimental'naya psikhologiya (Experimental Psychology).
   Moscow, I.L., 1950.

4. Gurovskiy, N.N. Gigiena i sanitariya. No. 3, 1959, p. 27.

5. Karchmazh, S.A. Vliyaniye obshchey vibratsii na uroven' potrebleniya
   kisloroda i uslovnoreflektornuyu deyatel'nost' zhivotnykh (The Effect
   of General Vibration on the Level of Oxygen Consumption and Conditioned-
   Reflex Activity of Animals). Author's abstract of candidate's disser-
   tation. Leningrad, 1962.

6. Leshli, K.S. Mozg i intellekt (The Brain and the Intellect). Moscow-
   Leningrad. Sotsekgiz., 1933.

7. Livshits, N.N. and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov
   kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The
   Effect of Space Flight Factors on Functions of the Central Nervous
   System). Moscow, "Nauka", p. 68.

8. Livshits, N.N. and Ye.S. Meyzerov. In the book: "Vliyaniye faktorov
   kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The
   Effect of Space Flight Factors on Functions of the Central Nervous
   System). Moscow, "Nauka", 1966, p. 236.

9. Livshits, N.N. and Ye.S. Meyzerov. In the book: "Nekotorye voprosy
   kosmicheskoy neyrofiziologii" (Some Questions of Space Neurophysiology).
   Moscow, "Nauka", 1967, p. 159.

10. Livshits, N.N., Ye.S. Meyzerov, R.M. Zakirova and V.A. Tikhaya. In the
    book: "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions
    of Space Neurophysiology). Moscow, "Nauka", 1967, p. 169.

11. Luk'yanova, L.D. In the book: "Vliyaniye ioniziruyushchikh izlucheniy
    i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy"
    (The Effect of Ionizing Radiations and Dynamic Factors on Functions of
    the Central Nervous System). Moscow, "Nauka", 1964, p. 60.

12. Luk'yanova, L.D. and Ye.P. Kazanskaya. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 81.

13. Luk'yanova, L.D., A.V. Kol'tsova, Ye.S. Meyzerov and Ye.P. Kazanskaya. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 105.

14. Luk'yanova, L.D. and V.Ya. Klimovitskiy. In the book: "Nekotorye voprosy kosmicheskoy neyrofiziologii" (Some Questions of Space Neurophysiology) Moscow, "Nauka", 1967, p. 145.

15. Mikheyeva, L. Tezisy dokl. 15-y itogovoy nauchnoy konf. studencheskogo nauchn. obshch-va med. in-ta (Theses of Reports of the 15th Concluding Scientific Conference of the Student Scientific Society of the Medical Institute). Perm., 1955, p. 30.

16. Pavlov, I.P. Reply to physiologists and psychologists. Poln. sobr. soch. (Complete Collected Works). Moscow-Leningrad. Izd-vo AN SSSR, No. 3, Book 2, 1951, p. 175.

17. Plokhinskiy, N.A. Biometriya (Biometry). Moscow, MGU, 1970.

18. Skachedub, R.V. In the book: "Doklady i tezisy 2-y Ural'skoy konf. fiziologov, biokhimikov i farmakologov" (Reports and Theses of the 2nd Ural Conference of Physiologists, Biochemists and Pharmacologists). Perm., 1957, p. 60.

19. Terent'yev, V.R. Zhurn. vysshey nervn. deyat. Vol. 9, No. 6, 1959, p. 649.

20. Levinson, B.I. J. Compar. Physiol. Psychol., No. 45, 1952, p. 140.

21. Nadel, A.B. In: Unusual Environments and Human Behavior. London, 1963, p. 379.

22. Schoenburn, R.L. and W.R. Adey. Rad. Res. Suppl., No. 7, 1967, p. 423.

# III

## ROLE OF THE TIME FACTOR
## IN REACTIONS OF THE CENTRAL NERVOUS SYSTEM
## TO RADIATION

## DEPENDENCE OF THE EFFECT OF GENERAL GAMMA-
## RADIATIONS ON CEREBROSPINAL REFLEXES OF GUINEA PIGS
## ON DOSE RATE

M. A. Kuznetsova

Study of the role of the time factor in radiation reactions of the central nervous system is very important not only to reveal mechanisms of pure radiation effects. In practical activity the human body is usually exposed to a whole complex of forces. With the development of astronautics there is an ever increasing probability of radiations complicated by a number of nonradiation effects. Studies in recent years [2, 3, 6, 7, 13] have shown that the factor of time plays an important role in these effects. Therefore, establishment of the dependence of radiation reactions of the central nervous system on dose rate is of no small value. At the same time, results obtained with regard to this question are somewhat contradictory.

Studies of higher nervous activity and ohmic resistance of the brain of rats, as well as vestibulotonic reactions in guinea pigs, conducted by N. N. Livshits, Ye. S. Meyzerov and Z. I. Apanasenko, led the authors to assume that with sublethal and minimally-lethal doses of radiation, lack of a direct relation between the damaging effect of radiation and dose rate is the rule for different sections of the central nervous system. In some cases there is even an inverse dependence on the time factor [1, 2, 9, 10, 11, 12].

This assumption is also verified in the literature. A. V. Lebedinskiy and Z. N. Nakhil'nitskaya [8], comparing the tests of M. Ye. Khozak which applied fractional radiations with those of A. A. Grafov and V. Ye. Maklashevskiy who used single general radiations in doses of 600 and 650 r, concluded there were more severe changes in higher nervous activity with fractionated forces. Our own

studies of unconditioned reflex motor activity in rabbits in 1961 led us to a
similar conclusion [4]. Fractionated radiation, produced for four weeks, caused
changes in the latent period of the defense flexor reflex of the hind limb of a
rabbit, statistically reliably not differing from those after a single radiation
in the same dosage. The results we obtained in 1967 contradicted these data and
the above assumptions. The radiobiological effect on change in the functional
state of the spinal section of the central nervous system showed a clear direct
dependence on dose rate. A study of the strength of threshold stimulation and
the latent period of unconditioned defense motor reactions of guinea pigs showed
that a single radiation with a high dose rate (260 r/min) was perceived by the
nervous system as analogous to high-intensity radiation, a single radiation
with a low dose rate (52 r/min) as a medium-intensity factor and fractionated
radiation (100 r × 5) as a low-intensity factor. Therefore, spreading the dose
of radiation out in time moderated damage to the tested reflex arc [6].

There is the highest interest in the discrepancy between our results and
the data of Z. I. Apanasenko, as experiments in both cases were made on the same
kind of animals and with identical kind of radiation in the same dosage.*. It
seems to us that the most probable cause of this difference is different timing
of the radiation dose. In our study there was a five-fold difference in dose
rates between the two kinds of single radiation; in the tests of Z. I. Apana-
senko it was fourhundred-fold. Fractionated radiation was a completely differ-
ent kind of force than prolonged radiation. It was, therefore, advisable to
study the change in unconditioned reflex motor activity of guinea pigs under the
influence of prolonged radiation with the same dose rate as in the experiments
of Z. I. Apanasenko. This would make it possible to test the assumption: is a
different form of supplying radiant energy actually the reason for a different
role of the time factor in radiation changes in the functional state of the
vestibular and spinal sections of the central nervous system.

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*Comparison of our results in 1961 and 1967 is difficult because of the
great diversity of experimental conditions: different kinds of animals (rabbits
and guinea pigs), different total radiation dose (400 and 500 r), differing
strength (9 and 52 r/min) and differing dose breakdown (20 r x 20 and 100 r x 5),
some difference in the radiation force (x-rays and $Co^{60}$ radiation) and test indices
(use of one and three gradations of pain stimulation).

We must point out that study of the effect of 14-hour radiation is by itself of interest for space biology, as its length closely approaches that of a solar flare.

## Method

The study was conducted on 23 male guinea pigs weighing 350-500 g, distributed into three groups. One group of animals (11 guinea pigs) was exposed to general single radiation in a dose of 554 r at a dose rate of 137 r/min.; another group (6 animals) was exposed to the same dose of radiation at a dose rate of 0.6 r/min. The nearly 14 hours of uninterrupted radiation of this group of animals occurred during the evening and night. Radiation in both cases was by means of $Co^{60}$. The third group of animals (6 guinea pigs), serving as the control, was kept under the same conditions as the test groups but not exposed to radiation.

The indices of the functional state of the cerebrospinal reflex arc were the threshold of excitability and the latent period of the unconditioned defense general motor reaction in response to electric skin stimulation of the hind paw of the animals. The latent period was recorded with accuracy to 0.5 m/sec.

The method of recording test indices and the schedule of the experiments have been described in previously published works [5, 6]. As stimuli we used three gradations of a direct current. In order to exclude the effect of sharp changes in thresholds of excitability on reflex responses, we used stimuli of a constant physiological strength.

1. Weak stimulus — always equal to the established threshold value.

2. Medium stimulus — always equal to the threshold value multiplied by 6, but not over 4 mA.

3. Strong stimulus — always equal to the threshold value multiplied by 10, but not over 5 mA.

After the limits of fluctuations of test indices were established in two weeks (4-5 tests), the animals were exposed to appropriate forces. The animals were examined 1, 2, 3, 5, 7, 10, 12 and 15 days after the force. At the same time we were studying these parameters we were observing the morphological state of peripheral blood and the clinical state of the animals. To compare results

from animals with different initial levels and variable test parameters, every absolute value measured after the force was expressed in percent of deviation from the average initial value of this parameter. Calculated percentage deviation was divided by the average group variance of these values before the force. Results were subjected to statistical analysis.

## Results

General single radiation in a dose of 554 r at a dose rate of 137 r/min. caused in all animals (with the exception of guinea pig No. 10, Fig. 4) a depression of the tested reflex activity, expressed by an increase in latent periods of reactions to all three kinds of stimulation (compared with the control, Fig. 1).

In the majority of animals (Fig. 2) this depression occurred against a background of regular force ratios between reflex responses to stimuli of various intensity. As a rule, the latent period of reactions to a weak stimulus was increased most and that of a strong stimulus least. Changes in the latent period of reactions to a medium strength stimulus occupied an intermediate position. Only the day before or the actual day of death, when maximum increase in test indices was recorded, was a tendency noted toward a disturbance of regular force ratios between reactions to medium and strong stimulation.

Inhibition of reflex activity in guinea pigs No. 9 and 20 (Fig. 3) was of a different kind. In these animals throughout the entire observation inhibition of reactions to strong stimulation was more significant than reactions to the other two stimuli. Between reflex responses to stimulation of various strength, therefore, a tendency toward disturbance of the regular force ratios was noted at a low level.

As seen from Figs. 2 and 3, inhibition of reflex activity developed gradually. In the majority of animals (see Fig. 2) in the first three days of radiation latent periods either remained within the limits of the initial level or showed a tendency toward shortening. One exception is the very slight increase in the latent period of reactions to a weak stimulus on the 2nd day of radiation. A tendency toward increased reflex activity was most clear on the first day of observation, i.e. the day of radiation. In guinea pigs No. 9 and 20 (Fig. 3) this tendency was slightly weaker. If the latent periods of reactions to some
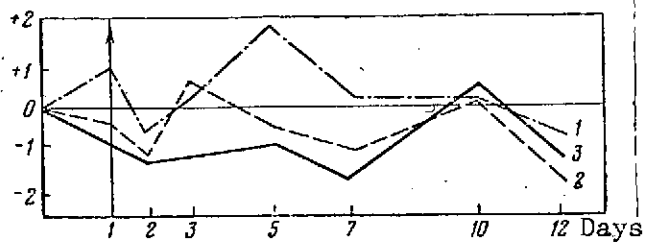
Figure 1. Changes in the average latent period of unconditioned defense motor reactions to weak (1), medium (2) and strong(3) stimuli in the control group of animals.|

Vertically — test index (in percentage deviation from average initial background, divided by average group variance before force). Average initial level on graph = 0, average variance before force = ± 1; arrow–day of radiation.|

kinds of stimulation remained within the limits of the initial level or even were significantly shortened, the same indices of reactions to other kinds of stimulations increased markedly.

As already indicated above, the change in test parameters in guinea pig No. 10, exposed to similar radiation (Fig. 4), was completely singular. In this animal throughout the entire period of observation an increase was noted in reflex conductivity with a tendency toward disturbance of the force law at a high level. Latent periods of reactions to a weak stimulus were shortened markedly during the entire observation and latent periods to the two other stimuli were either shortened less (in the first two days) or practically did not go beyond the bounds of the initial level.
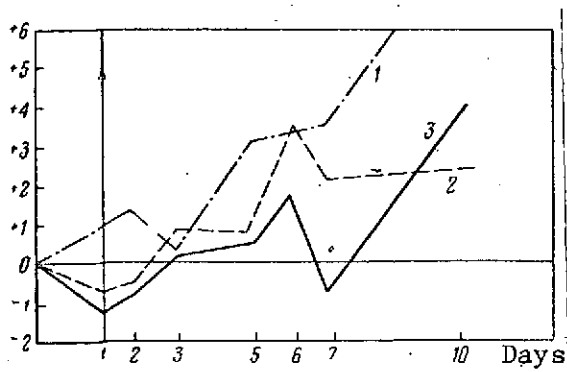


Figure 2. Changes in average latent period of unconditioned defense motor reaction in guinea pigs No. 4, 7, 8, 13, 16, 17, 18 and 19 after acute radiation |
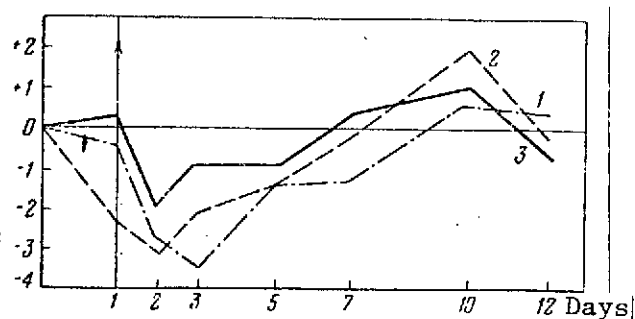
Symbols same as in Fig. 1.
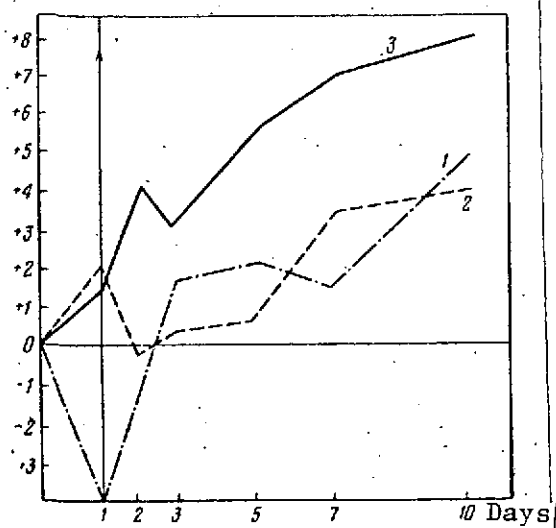
Figure 3. Changes in average latent period of unconditioned-defense motor reaction in guinea pigs No. 9 and 20 exposed to acute radiation.

Symbols same as in Fig. 1
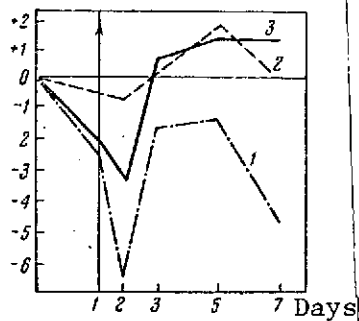
Figure 4. Individual changes in the latent period of unconditioned-defense motor reaction in guinea pig No. 10 exposed to acute radiation.

Symbols same as in Figure 1.

Figure 5. Change in average threshold stimulation in animals exposed to acute radiation.

1 — entire test group of animals; 2 — guinea pigs No. 19 and 17; 3 — individual changes in guinea pig No. 8; 4 — control

Other symbols same as in Figure 1.
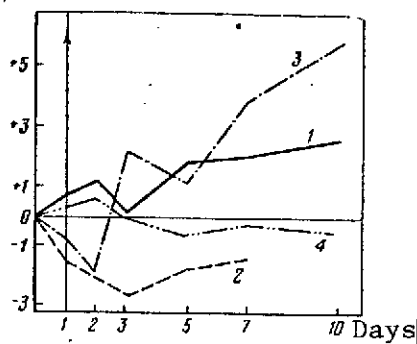
Change in reflex excitability under the influence of acute radiation was of two kinds. In the majority of animals (as evident in the example of guinea pig No. 8) the strength of threshold stimulation in the first two days of observation showed a tendency toward reduction, and later gradually increased, reaching significant values by the time of death (Fig. 5, 3). And only in two guinea pigs during the entire period of examination was increased reflex conductivity recorded. Even in the predeath period the strength of threshold stimulation was markedly lower than the initial level (Fig. 5, 2).

Changes in unconditioned reflex activity under the influence of prolonged radiation were much more varied than with acute radiations. In guinea pigs Nos. 2, 5 and 12 (Fig. 6), throughout the entire observation period an increase was recorded in reflex conductivity with a tendency toward disturbance of regular force ratios between reflex responses to different stimulation according to the type of equalizing phase at a high level. The latent period of reactions to a strong stimulus was shortened less than reactions to the other two stimuli. Test indices in the predeath period returned to the initial level.

In the other three animals (Fig. 7), throughout the entire period of examination wavelike fluctuations were noted in reflex conductivity. Reduction

Figure 6. Changes in the average latent period of unconditioned-defense motor reaction in guinea pigs Nos. 2, 5 and 12 after prolonged radiation.
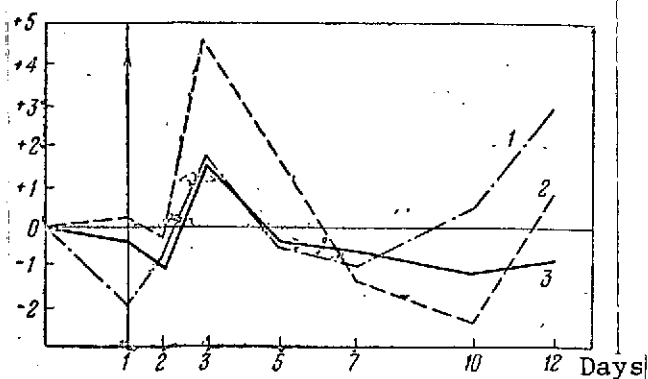
Symbols same as in Fig. 1.



Figure 7. Changes in the average latent period of unconditioned-defense motor reaction in guinea pigs Nos. 1, 11 and 14 after prolonged radiation.

Symbols same as in Fig. 1.

`·5` `·3` `·1` `0` `·1` `·3`

`2` `1` `3`

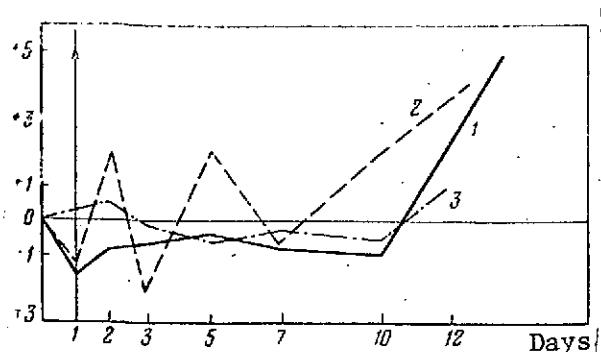`1  2  3   5   7    10   12   Days`

Figure 8.   Changes in average threshold stimulation in animals exposed to prolonged radiation.

1 — entire test group of animals;
2 — individual changes in guinea pig No. 11;  3 — control

Other symbols same as in Fig. 1.

of test indices alternated with their increase.  Here reactions to a medium stimulus were most significantly inhibited.  Changes in reactions to the other two stimuli were small.

In the change in reflex excitation under the influence of prolonged radiation in the majority of animals there was a tendency toward increase which was most pronounced on the day of radiation (Fig. 8, 1) and only in guinea pig No. 11 on the 3rd and 5th day of radiation was an increase recorded in the strength    /135 of threshold stimulation (Fig. 8, 2).  The day before or the day of death itself reflex excitation in the majority of cases was significantly reduced.  Despite these changes, the difference from the control (Fig. 8, 3), according to the criterion of median, was unreliable.

<u>Discussion of results</u>

At the present time it can be established that ionizing radiations cause two-phase changes in the functional state of various sections of the nervous system.  The initial increase of excitability is replaced by its progressive inhibition.  With rather weak forces only the first phase can be recorded.  As the intensity of the force increases, the second phase becomes clearer and proportionally larger and the first phase, less pronounced.  Often with large doses of radiation it can be detected only in the first few minutes after the force.

These studies also reveal two-phase changes in the functional state of the spinal section of the central nervous system in response to $Co^{60}$ gamma radiation.  However, the length and severity of both phases were different with different kinds of radiation.

In animals exposed to prolonged radiation, increased conductivity of the tested reflex arc predominated. Such a state during almost the entire period of observation was noted in half of the animals (see Fig. 6). In the other half incomplete inhibition of test reactions periodically alternated with their increase (see Fig. 7).

After acute radiation the phase of depression predominated in the change in the functional state of the spinal section of the central nervous system. Significant inhibition of reactions of all three kinds of stimulation was recorded in practically all animals throughout the entire period of observation, beginning with the 2-3rd day after radiations (see Fig. 2 and 3) and only in guinea pig No. 10 (see Fig. 4) was a marked increase noted in unconditioned reflex activity.

This analysis shows that as doses of radiation are spread out in time the severity and length of the phase of increased reflex conductivity increased and the phase of its depression decreased, indicating the moderating effect of prolonging the dosage. The results were statistically analyzed according to the criterion of median. It is known that this criterion is distinguished by low sensitivity. It verifies the statistical reliability of results only in those cases when they are of the same kind and changes in medians of test indices are significant. When changes in this index have a wavelike character and fluctu- /136 ate in the area of both positive and negative values and, therefore, deviation of the median from the initial level is very small reliability of evident changes is not found according to this criterion. Therefore, statistical reliability of these results in our study was verified only for the group of animals exposed to acute radiation. Changes in test indices after prolonged radiation, although significant, were not of the same type. Therefore, no reliability of difference in changes of test indices in this group of animals or in the control could be detected according to the criterion of median. However, the fact itself indicates less depression of the effect of prolonged radiation (table).

A comparison of changes in reflex excitability in test groups of animals also indicates a more depressed effect of acute radiation. While the strength of threshold stimulation remained practically unchanged after prolonged radiation, strong radiations caused a statistically reliable increase in the test index (see Fig. 5, 1 and Fig. 8, 1).

MEDIANS OF LATENT PERIODS OF UNCONDITIONED-DEFENSE MOTOR REACTION
IN GUINEA PIGS EXPOSED TO VARIOUS KINDS OF GAMMA-RADIATION
IN TOTAL DOSAGE OF 500-554 r

| Kind of force, dosage, dose rate | Stimulus | | |
|---|---|---|---|
| | weak | medium | strong |
| Single radiation, 500 r 260 r/min | +1.85 | +1.4 | +0.86 |
| Single radiation, 554 r, 137 r/min | +1.98 | +1.1 | +0.74 |
| Single radiation, 500 r, 52 r/min | +1.7 | +1.2 | −0.49 |
| Single prolonged radiation, 554 r, 0.6 r/min | −1.15 | −0.99 | −0.27 |
| Fractionated radiation, 500 r, 100 r x 5 | −1.15 | −0.23 | −0.96 |

| Kind of force | Stimulus | | |
|---|---|---|---|
| | weak | medium | strong |
| Controlled radiation, dosage 52 and 260 r/min | +0.57 | −0.2 | −0.51 |
| Controlled radiation, dosage 137 and 0.6 r/min | +0.24 | −0.91 | −0 |
| Controlled fractionated radiation | −0.51 | −0.85 | −0.45 |

In an earlier work [6] we analyzed in detail data obtained with gamma-
radiation of animals in a total dose of 500 r, fractionated (100 r x 5) and in
a single dose at dose rates of 260 and 52 r/min. Results clearly indicate that
as the length of radiation increased the radiation reaction of the spinal sec-
tion of the central nervous system was moderated. This study makes it possible
to compare the effect on these same indices of radiation in a similar dosage
(554 r) with dose rates of 137 and 0.6 r/min with the effects produced previously.
The table shows that medians of latent periods of unconditioned-defense motor
reactions of animals exposed to both prolonged (this report) and fractionated

ionizing radiations [6] lie in the area of negative values. Medians of these data for groups of animals exposed to acute radiation are shifted toward positive deviations. Here the most significant shifts are noted in the group of animals radiated at dose rates of 137 and 260 r/min [5] and least significant in the group radiated at a dose rate of 52 r/min [6]. Thus, results of the study of changes in latent periods of defense motor reactions, obtained in this work, completely agree with data published earlier. We must, however, note that only differences between animals exposed to acute radiation and those exposed to radiation spread out in time were reliable according to the criterion of median. The reliability of differences between the effects of prolonged and fractionated radiations, as well as between the effects of different kinds of acute radiations, were not verified according to this criterion.

Analysis of changes in the state of the tested reflex arc from the position of the scheme of N. V. Golikov* also leads to a conclusion in perfect agreement with those published earlier.

From Fig. 9 it is evident that the action of acute radiations was distinguished by marked shortening (up to complete absence) of states of stationary excitation (see I-III, 2 with A and B, 2) and the presence of all three phases of parabiosis (I-III, 3, 4, 5). The percent of cases with the third phase in all three groups of animals after acute radiation was approximately the same (15-18%). The difference between groups was basically unequal presence of the other two parabiotic phases. After acute radiation with a dose rate of 260 r/min the functional state of the tested reflex arc changed primarily according to the type of second /138 phase of parabiosis (see Fig. 9, I), while after the other two kinds of acute force this change occurred with a predominance of the first and second phases (see Fig. 9, II and III). The percent of the latter in animals radiated with a dose rate of 137 r/min was slightly higher (although unreliable) than in those radiated at 52 r/min.

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*Phase stages of parabiosis, according to N. V. Golikov, are characterized by certain relations between the state of reflex excitability (strength of threshold stimulation) and physiological lability (in our case it is reflected by changes in the latent period of reactions to a strong stimulus). Phases of parabiosis, according to N. V. Golikov, and the application of this scheme to our indices were discussed in more detail in earlier published works [6].

Radiation spread out in time, unlike an acute force, was characterized
by the practical absence of the third phase of parabiosis (see Fig. 9, IV and
V, 5) and increase in the number of cases of stationary excitation (see Fig. 9,
IV and V, 2).  This increase was greater in the group of animals exposed to
fractionated radiation.  The percent of these states in this group increased in
comparison with the control 4.5 times, while in the group exposed to prolonged
radiation it increased only 1.4 times.  The weaker effect of fractionated radi-
ation is also indicated by the fact that, afterward, basically only the first
phase of parabiosis was recorded, while after prolonged radiation the second
parabiotic phase predominated.

This analysis shows that as the dose of radiation is spread out in time
the number of cases of late parabiotic states is reduced and the percent of tests
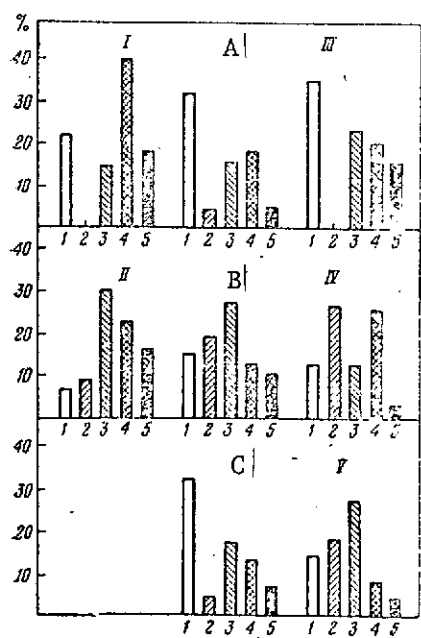


Figure 9.  Distribution of parabiotic
states in test groups of animals
exposed to different kinds of gamma
radiation.

1 — state of physiological lability
and reflex excitability within limits
of the initial level;  2 — state of
stationary excitation; 3, 4, 5 —
first, second and third phases of
parabiosis;  A — controlled single
radiation at dose rates of 260 and
52 r/min;  B — same, dose rates of
137 and 0.6 r/min.;  C — controlled
fractionated radiation;
I-IV — in animals exposed to single
radiations at dose rates of 260, 137,
52 and 0.6 r/min;  V — in animals
exposed to fractionated radiation.

Vertically — number of tests (in %)
with the presence of corresponding
functional states.

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with the presence of early stages of parabiosis is increased (according to N. V.
Golikov).

Figure 10. Change in average number of leukocytes in 1 mm$^3$ of peripheral blood of animals.

1 — control; 2 — animals exposed to prolonged radiation; 3 — animals exposed to acute radiation.

Other symbols same as in Fig. 1.
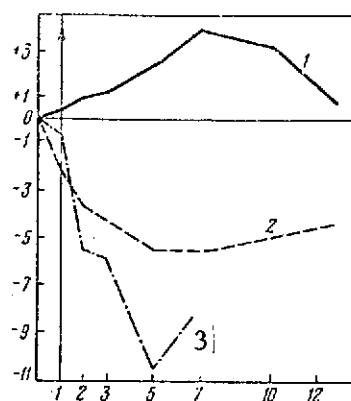


Functional shifts in the tested reflex arc, therefore, evaluated by the change in the ratio of states of reflex excitability and physiological lability, completely verify the conclusion that in the tested range of doses and dose rates, radiation disturbances of the spinal section of the central nervous system are moderated as the radiation dose is spread out in time (regardless of the kind of timing). This moderation is more appreciable the larger the interval of time over which radiant energy is spread.

In comparing survival of animals and the severity of radiation sickness a direct dependence is also seen on the time factor and according to these indices the least effective was prolonged radiation. Leukopenia in the group of animals after acute radiation was greater than in those exposed to prolonged radiation (Fig. 10). Although in both cases all animals died, the average length of life after prolonged radiation was greater (13 days) than after acute (9, 8 days).

These results agree completely with those we obtained earlier [6] as well as with numerous literature data.

## Conclusions

1. Prolongation of radiation in dosage of 550 r (dose rate 0.6 r/min) moderated tested radiobiological effects.

2. Comparison of these results with previously published data verifies the conclusion that there was a direct effect of the time factor on these indices with the kinds and doses of radiation we used.

3.  Moderation of radiation disturbances of the functional state of the
spinal section of the central nervous system does not depend on the way radiant
energy is supplied in time.  It is greater the longer the interval of time over
which radiation is spread.

## REFERENCES

1.    Apanasenko, Z.I.  Radiobiologiya, Vol. 1, No. 1, 1961, p. 45.

2.    Apanasenko, Z.I.  In the book:  "Vliyaniye faktorov kosmicheskogo poleta
      na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight
      Factors on Functions of the Central Nervous System).  Moscow, "Nauka",
      1966, p. 197.

3.    Bondina, V.A., I.B. Il'inskaya and N.V. Korostovtseva.  In the book:
      "Aktual'nye voprosy perelivaniya krovi" (Current Questions of Blood
      Transfusion).  Leningrad, Medgiz., No. 6, p. 41.

4.    Kuznetsova, M.A.  Radiobiologiya.  No. 1, 1961, p. 58.

5.    Kuznetsova, M.A.  In the book:  "Vliyaniye ioniziruyushchikh izlucheniy
      i dinamicheskikh faktorov na funktsii tsentral'noy nervnoy sistemy"
      (The Effect of Ionizing Radiations and Dynamic Factors on Functions
      of the Central Nervous System).  Moscow, "Nauka", 1964, p. 103.

6.    Kuznetsova, M.A.  In the book:  "Nekotorye voprosy kosmicheskoy neyro-
      fiziologii" (Some Questions of Space Neurophysiology).  1967, p. 93.

7.    Kruk, I.N.  In the book:  "Deystviye ioniziruyushchikh izlucheniy na
      zhivoy organizm" (The Effect of Ionizing Radiations on the Living
      Organism).  Kiev. Gosmedizdat UkSSR, 1960, p. 454.

8.    Lebedinskiy, A.V. and Z.N. Nakhil'nitskaya.  Vliyaniye ioniziruyushchikh
      izlucheniy na nervnuyu sistemu (The Effect of Ionizing Radiations on
      the Nervous System).  Moscow, Atomizdat., 1960.

9.    Livshits, N.N.  Deystviye ioniziruyushchikh izlucheniy na biologicheskiye
      ob'yekty (The Effect of Ionizing Radiations on Biological Objects).
      Moscow, Izd-vo AN SSSR, 1954, p. 84.

10.   Livshits, N.N.  Trudy In-ta biol. fiziki., No. 1, 1955, p. 63.

11.   Livshits, N.N.  Vliyaniye ioniziruyushchikh izlucheniy na funktsii
      tsentral'noy nervnoy sistemy (The Effect of Ionizing Radiations on
      Functions of the Central Nervous System).  Moscow, Izd-vo AN SSSR, 1961.

12.   Livshits, N.N. and Ye.S. Meyzerov.  Radiobiologiya.  Vol. 4, No. 4, 1963,
      p. 460.

13.   Pushnitsyna, A.D.  Radiobiologiya.  Vol. 6, No. 2, 1962, p. 847.

# ON THE ROLE OF THE TIME FACTOR
## IN RADIATION REACTIONS OF THE VESTIBULAR ANALYSOR
## AND SPINAL SECTION OF THE CENTRAL NERVOUS SYSTEM

### Z. I. Apanasenko, M. A. Kuznetsova

In previous studies we have shown that in radiation effects in vestibular and spinal sections of the central nervous system of guinea pigs, a reduction in the dose rate of radiation plays an opposing role. Study of unconditioned-defense motor reactions clearly revealed the moderating effect of fractionation of gamma-radiation [7]. Disturbances of vestibulotonic reflexes after prolongation of an analogous dose not only were not reduced, but according to several indices were even greater than after acute radiation [1]. As the experiments were conducted on the same kind of animals, with the same kind of radiation in equal doses, it seemed to us that the most probable cause of this discrepancy of results was a different way of supplying the radiant energy. It is true that moderation of radiation disturbances in the spinal section of the central nervous system was also noted in the case of a single gamma-radiation when the dose rate was reduced [7]. However, the difference in dose rates of compared single radiations in this instance was 80 times less than in the study of radiation changes in vestibulotonic reactions. The dependence of the role of the time factor in radiation effects on the range of doses used and their rates is widely known in the literature [5, 9, 13, 17, etc.].

Something similar was also suggested by data we obtained in a study of rabbits in 1961. In this series of experiments we used single and fractionated x-rays at a dose rate of 9 r/min. with the total dosage being 400 r. Fractional radiation was produced 5 times a week in single doses of 9 r. Results indicated identical shifts in unconditioned-defense flexor reflexes in animals exposed to both kinds of radiation.

For the purpose of proving the above assumption, a study was made of the effect on unconditioned-reflex activity of gamma-radiations prolonged in the same way as in the study of vestibulotonic reflexes. Data of this study are cited in the preceding article in this collection. They clearly indicate that moderation

of the radiation reaction in the spinal section of the central nervous system of guinea pigs with the exposures and doses we used does not depend on the way radiant energy is supplied in time.

Prolongation of radiation reduces radiation changes in unconditioned reflex activity, unlike disturbances in the vestibular apparatus.

The literature indicates that with the same dose range and rates, not only different organs and systems react dissimilarly [11, 12], but also reactions of various sections of the central nervous system can be different. Brissell [15] studied weight changes of the brain of white rats using single and fractional x-rays in a total dosage of 150 rad (dose rate 40 rad/min.). Fractional forces were produced five times at intervals of three hours in single doses of 30 rad. Studies showed that with a single radiation the weight of the prosencephalon is reduced more and with a fractionated force that of the cerebellum.

This leads to the conclusion that with the same dose range and rates, the time factor can play different roles in radiation shifts in spinal and vestibular sections of the central nervous system. To prove this assumption we felt it advisable to compare radiation changes in these sections of the central nervous system in the same animals .

<div align="center">Method</div> <div align="right">/142</div>

The study was conducted on male guinea pigs weighing 250-300 g. The functional state of the vestibular analysor was evaluated by electromyographic characteristics of the vestibulotonic reflex. The vestibular apparatus was stimulated by metered swinging of the animal around the long axis of the body in a special unit. The characteristics of electromyograms were determined, recorded from the group of extensor muscles of the hind limb in a state of relative rest, during stimulation and immediately afterward. According to the classic studies of Magnus [18], the vestibular reflex in the muscle of the extremity which develops during a change in body position in relation to the horizontal axis originates in sensitive patches of the utricles.

As an index of the functional state of the cerebrospinal reflex arc we selected the latent period of the unconditioned defense general motor reaction in response to electric skin stimulation of the hind paw of the animal. As stimulation we used three gradations of a direct current. At the present time

it can be considered established that change in the conductivity of spinal reflex arcs is determined and, therefore, also reflects a change in their central part [2, 3, 4, 16, 19, 20] consisting primarily of disturbance of synaptic transfer [14, 19, 20] at the level of afferent and internuncial neurons [8].

The method of recording test indices, the schedule of experiments and analysis of results are described in previously published works [1, 4, 7]. At the same time these parameters were being determined we observed peripheral blood, weight and the clinical state of the animals. After we established stable values for test indices the animals were exposed to $Co^{60}$ radiation (dosage 500 r, dose rate 0.6 r/min.). Continuous 14-hour radiation was produced during the night. Control animals were kept under the same conditions but exposed to no radiation. Examination of the animals began 2-2½ hours after radiation on the 1st, 2nd, 3rd, 5th, 7th, 10th, 12th, 15th and 20th days. Control animals were examined at the same times.

In 6 animals exposed to prolonged radiation both vestibulotonic and unconditioned-defense motor reactions were recorded. These results were compared with changes in analogous indices obtained earlier in 7 animals radiated once with the same dose but at a dose rate of 260 r/min [1 and 7].

To more accurately define the role of the time factor in radiation changes in vestibulotonic reactions, these indices were also studied in 16 more guinea pigs. Four were exposed to analogous prolonged radiation and 12 guinea pigs to /143 a single radiation of the same dosage but at a dose rate of 137 r/min. Spinal reflexes were not recorded in these animals. All results were subjected to statistical analysis by the criterion of median.

## Results

Change in unconditioned reflex activity under the influence of prolonged radiations* was of two kinds. In guinea pigs Nos. 22 and 26 (Figs. 1, 2, 1-2-3), killed after radiation, latent periods of reactions to all three kinds of stimulation were either shortened or did not go beyond the bounds of average group deviations before the force. Increased reflex conductivity was more pronounced in the first two days of observation. Fluctuations of the test index in reactions

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*The change in analogous indices in control animals is given in Fig. 1.

to all three kinds of stimulation were approximately the same, indicating preservation of the law of force.

In guinea pigs Nos. 23, 24, 27 and 29, surviving after radiation, tested indices in the first 10 days of observation were also either within the limits of the initial level (Fig. 3, 1 and 2) or showed a tendency toward shortening (Fig. 3, 3). On the 12th and 15th day inhibition of test reactions was noted. In a number of cases reactions to strong and medium stimuli were more strongly depressed, causing a disturbance of regular force ratios according to the type of equalizing phase at a low level. On the graph demonstrating changes in average values among this group of animals, such a disturbance can be seen on the 12th day of observation. By the 20th day of observation test indices showed a tendency toward normalization.

Fig. 4 gives change in unconditioned reflex activity in animals exposed to a single general radiation (dose rate 260 r/min.). In all animals without exception throughout the entire examination period depression of test reactions was recorded. It was greatest on the 2nd day after radiation and in the pre-death period. Only on the day of the radiation did test parameters not go beyond the limits of average group deviation before the force. Change in reflex conductivity emphasized regular force ratios. The latent period of reactions to a weak stimulus was increased most and for a strong stimulus least. Reactions to a medium stimulus occupied an intermediate position.

These experiments showed also that acute and prolonged radiations in the same dosage cause slightly different changes in test characteristics of the vestibulotonic reflex. Thus, spontaneous bioelectric activity of muscles in     /144 a state of relative quiet (Fig. 5) after acute radiation immediately decreases and remains low throughout the entire period of examination. Maximum reduction is attained by the 12th day after the force. In surviving animals a slow increase in myoelectric activity begins on the 15th day with gradual approach to     /146 the initial level. Prolonged radiation causes quite a sharp increase in spontaneous electric activity of muscles which is maintained throughout the first week after the force. By the 10th day myoelectric activity is significantly reduced; from the 12th day the reduction becomes the same as with acute radiation. With long radiation, therefore, spontaneous electric activity of muscles changes as much as in acute radiation (amplitude of deviation from initial
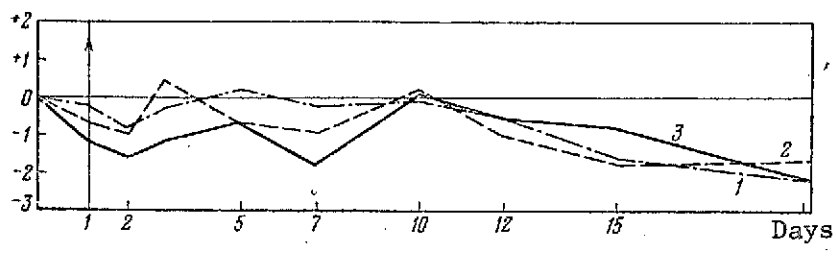
Figure 1. Changes in the average latent period of unconditioned-defense motor reactions to weak (1), medium (2) and strong (3) stimuli in the control group of animals.

Vertically — test index (in percentages of deviations from average initial background value, divided by average group variance before the force). Average initial level on graph = 0, average variance before force = ±1. Arrow — day of radiation.
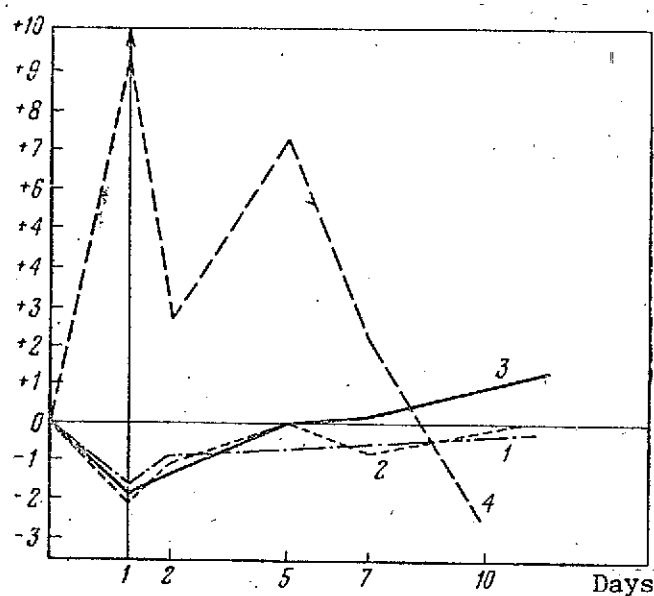


Figure 2. Change in the average latent period of unconditioned-defense motor reaction (1, 2, 3) and spontaneous electric activity of extensor muscles (4) in guinea pigs Nos. 22 and 26 after prolonged radiation.

Other symbols same as in Fig. 1.
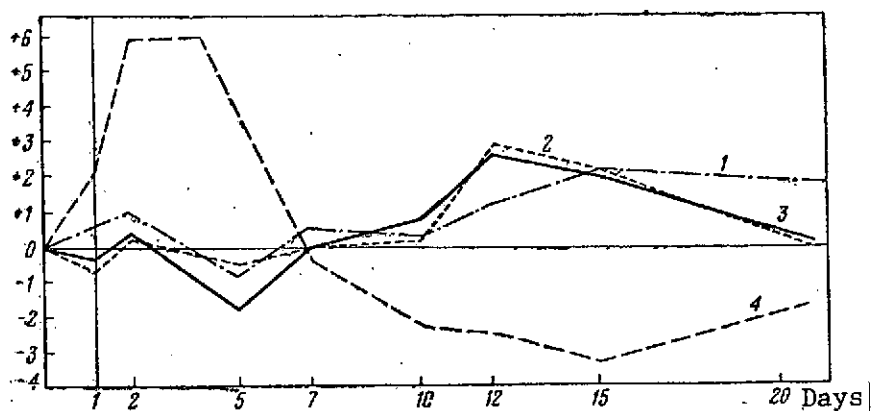
Figure 3. Change in average latent period of unconditioned-defense motor reaction and spontaneous electric activity of extensor muscles in guinea pigs Nos. 23, 24, 27 and 29 after prolonged radiation.

Symbols same as in Fig. 1, 2.
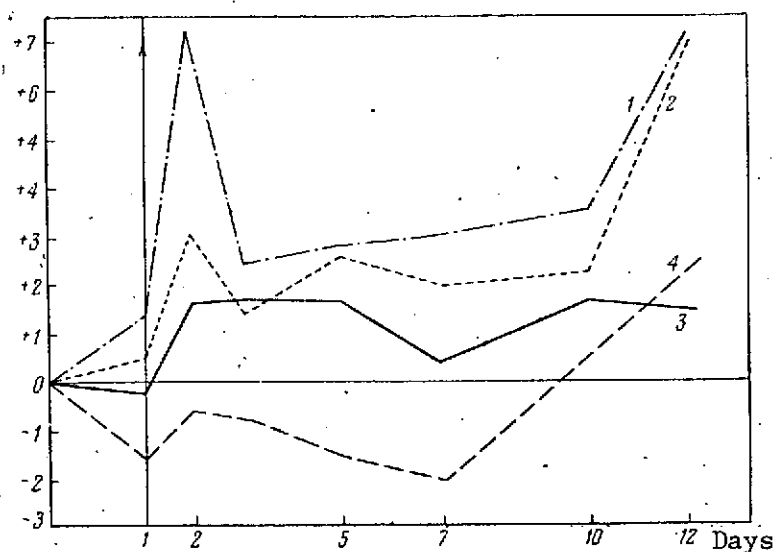
Figure 4. Change in average latent period of unconditioned-defense motor reaction and spontaneous electric activity of extensor muscles in guinea pigs exposed to acute radiation.

Symbols same as in Fig. 2.

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level in the first period is even significantly larger) but changes here have a pronounced two-phase character. As a result, differences between the effects of acute and prolonged radiation are statistically reliable (p<0.01). Also reliable is the difference from the control for both kinds of forces (p<0.001). The effects observed in different animals within each group are very similar. No essential deviation from the indicated character of changes was noted.

Reaction to adequate vestibular stimulation, without regard to its relation to the level of background electric activity (Fig. 6), changes under the influence of acute and prolonged radiations almost the same as spontaneous myoelectric activity itself. After acute radiation the level of reaction immediately decreases but after prolonged radiation changes again have a two-phase character. During the first week after the force, the reaction to adequate stimulation of the vestibular apparatus was significantly increased and from the 10th day sharply reduced. The reduction was also greater than with acute radiation. From the 15th day effects of both kinds of force became practically identical. Return to the initial level during the examination period, according to this index, was not observed. Curves reflecting changes after both kinds of radiation reliably differ from each other (p<0.05) and from the control (p<0.01). Effects are similar for all animals in each group.

The two-phase character of changes after prolonged radiation is also seen in the after-action of the tested vestibulotonic reaction (Fig. 7) when this is also considered without regard to background spontaneous electric activity. Here also during the first week total electric activity of muscles significantly increases but from the 10th day sharply decreases. After acute radiation the total electric activity of muscles in after-action is reduced in the first few days and remains so during the entire examination period. From the 10th day after the force the effects of both exposures practically coincide. The effects of acute and prolonged radiations statistically reliably (p<0.01) differ from each other only in the different direction of effects in the first period after the force. From the 10th day this difference becomes unreliable. According to the value of the changes, the effect of long radiation is not inferior to that of brief radiation and even slightly exceeds it. Changes are similar in all animals in each group; difference from the control is statistically reliable (p<0.05 and p<0.01).
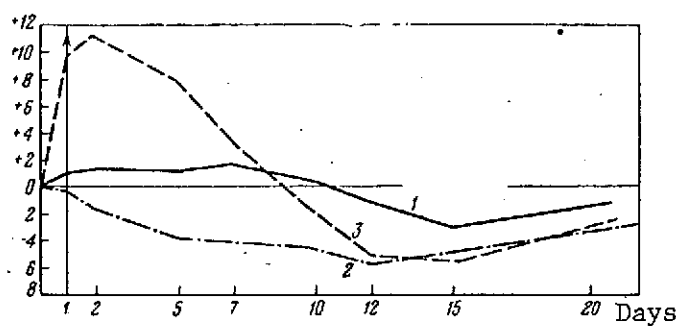
Figure 5. Change in spontaneous electric activity of extensor muscles of the hind limb of guinea pigs after acute and prolonged radiation in doses of 500 r.

1 — control;  2 — acute radiation (137 r/min);  3 — prolonged radiation (0.6 r/min.)
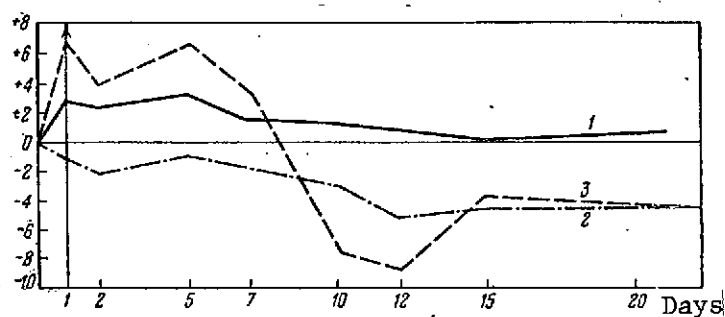
Other symbols same as in Fig. 1.



Figure 6. Change in electric activity of extensor muscles of the extremity during adequate stimulation of the vestibular apparatus after acute and prolonged radiation.

Symbols same as in Fig. 5.
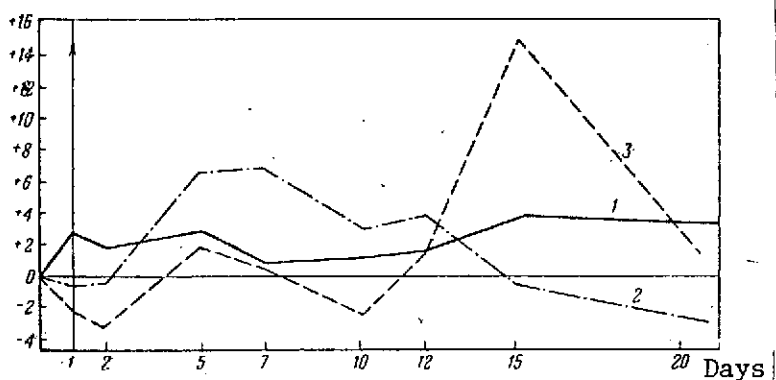Values calculated without regard to spontaneous electric activity of muscles.
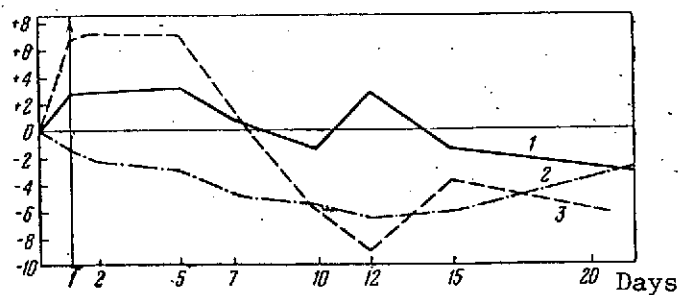


Figure 7. Change in electric activity of muscles in after-action of reaction to adequate stimulation of the vestibular apparatus after acute and prolonged radiation.

Symbols same as in Fig. 5
Values calculated without regard to spontaneous electric activity of muscles.

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Figure 8. Change in electric activity of extensor muscles of the extremity during adequate stimulation of vestibular apparatus after acute and prolonged radiation.

Symbols same as in Fig. 5.
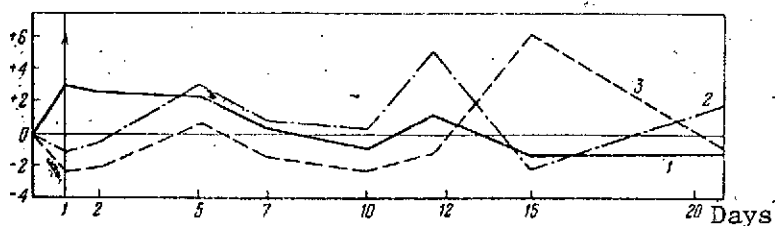Values calculated in relation to spontaneous electric activity of muscles.



Figure 9. Change in electric activity of muscles in after-action of reaction to adequate stimulation of the vestibular apparatus after acute and prolonged radiation

Symbols same as in Fig. 5
Values calculated in relation to spontaneous electric activity of muscles

However, if the reaction and after-action are represented as excess electric activity (in response to adequate stimulation) above the level of the background, also changing after radiation, then the following ratio will be seen. After acute radiation reaction to vestibular stimulation (Fig. 8) before the 12th day is on the average higher than in control animals, but after a prolonged force it is lower. After the 12th day a reverse phenomenon is observed: now the curve reflecting the effect of an acute force is below and that demonstrating the effect of prolonged radiation is above the curve re-

flecting change in the control. There is a change in the direction of the effects. For the first phase of changes greater predominance of inhibitory phenomena is typical of prolonged rather than acute radiation. In the second phase of postradiation changes the ratios are reversed. The reliability of differences between the effects of both forms of radiation is verified statistically ($p < 0.01$ with analysis of both phases of changes individually).

A completely analogous character of changes is also observed according to the level of electric activity in the after-action of adequate stimulation of the vestibular apparatus (Fig. 9). Here also during the first 12 days the total electric activity of muscles is on the average greater with acute radiation and with prolonged radiation less than in the control, i.e. there again is a greater predominance of inhibiting processes after a prolonged force. In the second phase of changes the ratios are reversed. When results are analyzed according to the criterion of median for each phase of changes individually, differences between the effects of acute and prolonged radiations are reliable ($p < 0.05$).

Strong postradiation changes in spontaneous electric activity can, perhaps, to some degree mask the true character of the effects of radiation on myoelectric activity during and after vestibular stimulation. It can, therefore, be assumed, for example, that during the first phase of changes the increase in spontaneous electric activity is so great that further increase of myoelectric activity in response to the test stimulation is unnoticed against this background. It is even possible that there is also some critical level of electric impulses for the tested physiological systems. Similar ratios were also observed with the effect of a number of other factors (vibration, centrifuging) on the vestibular analysor and have been discussed in previous works. However, in this case greater predominance of inhibiting processes after prolonged radiation is also verified by the character of changes in the latent period of the vestibulotonic reaction.

Changes in the latent period of the electromyographic reaction to adequate stimulation of the vestibular apparatus (Fig. 10) after both forms of radiation are qualitatively identical. In both cases there is a significant increase in the latent period of the reaction; however, after prolonged radiation it is much stronger than after acute. Only during the 12-15th days after a prolonged

force is the latent period slightly shortened to less than with acute radiation.

In this first phase of changes, therefore, when after a long exposure to radiation electric activity of muscles is reduced during and after vestibular
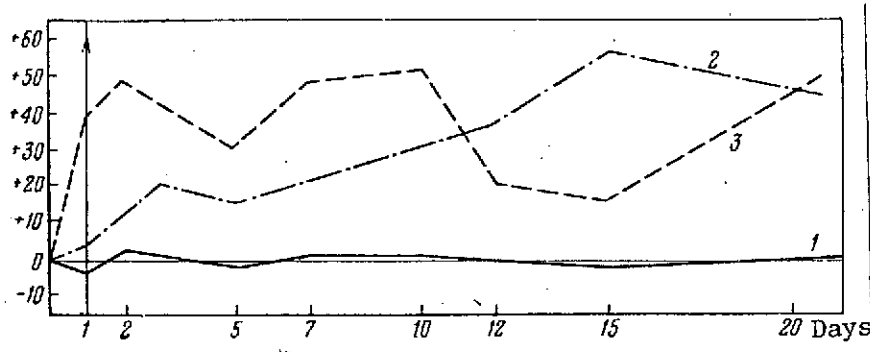
Figure 10. Change in the latent period of electromyographic reaction to adequate stimulation of the vestibular apparatus after acute and prolonged radiation.
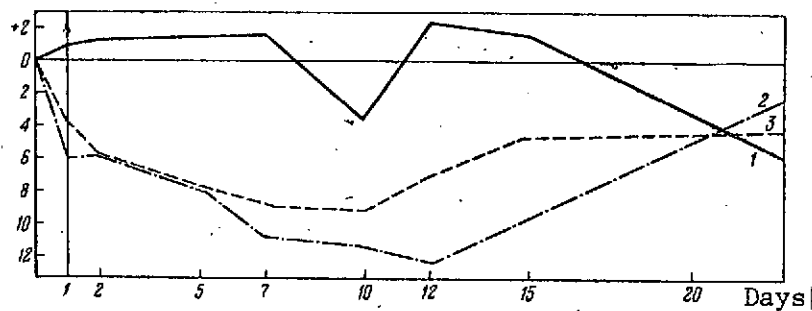
Symbols same as in Fig. 5.

Figure 11. Change in length of the after-action of electromyographic reaction to adequate stimulation of the vestibular apparatus after acute and prolonged radiation.

Symbols same as in Fig. 5.

stimulation, there is also the greatest increase in the latent period of the test reaction. This indicates that after prolonged radiation during this period of time inhibition is actually more severe than after an acute force. From the 12th day the second phase of changes is also noted here when greater predominance of inhibitory processes is observed after acute radiation. But on the 20th day the latent period of vestibulotonic reaction of guinea pigs exposed to a prolonged force again increases to the same level as with acute radiation. The difference between effects of different kinds of radiation is statistically
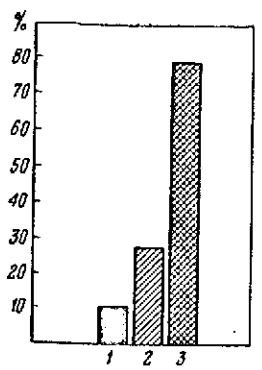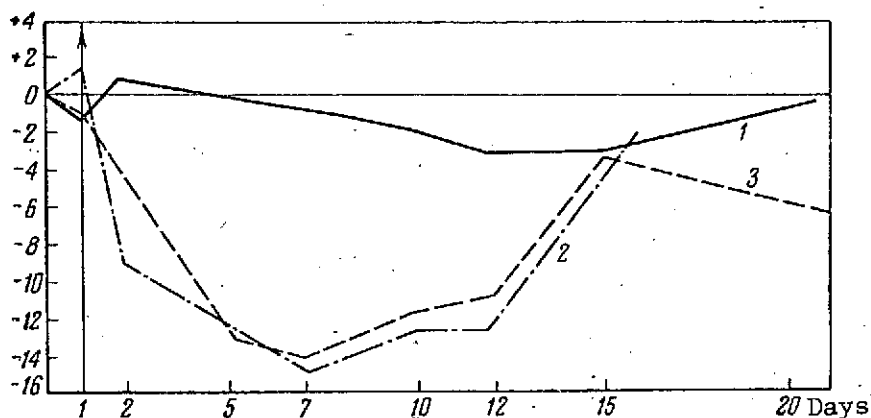
Figure 12. Diagram of survival of animals (in %)
by the 30th day after the force.

1 — radiation with a dose rate of 261 r/min.;
2 — same at 137 r/min; 3 — same at 0.6 r/min.

Figure 13. Change in the number of leukocytes per
1 mm$^3$ in peripheral blood of animals after acute
and prolonged radiation.

Symbols same as in Fig. 5.



reliable (p<0.01). Also reliable is difference from the control (p<0.001).

The length of after-action of the tested reaction (Fig. 11) is decreased
after both acute and prolonged radiation. However, here the effect of the
acute force is on the whole slightly stronger than that of long radiation.
The difference between the effects of both forces according to this index is
not very great, but it is statistically reliable (p<0.05); also reliable is
their difference from the control (p<0.001). During the first week after radi-
ation the length of the after-effect is shortened practically the same with
both exposures. In the period from the 10th to the 15th day the reduction of
the length of the after-action as the result of acute radiation is slightly
greater than that after a prolonged force. By the 20th day the effects of both
forms of radiation again equalize and a tendency toward normalization of values
is noted. The character of changes in the length of the after-action of the
tested reaction indicates that the effect of prolonged radiation is first the
same as that of acute, but after the first 7 days is reduced and becomes slightly
weaker than that of acute radiation.

Indices characterizing the state of the vestibular analysor, therefore, change after prolonged radiation most often to the same or even greater degree than after an acute force. Less severe changes with prolonged radiation occur only in some cases in the second period (from the 10-12th day) of time after the force.

The clinical course of radiation sickness is more severe in guinea pigs exposed to acute radiation. Their general condition is worse, intestinal disturbances, hemorrhages and other complications are greater, survival is significantly lower (Fig. 12). In animals exposed to long radiation survival was 80±12.7%. Among animals exposed to brief radiation only 27.3±13.4% lived. The difference is statistically reliable even with our data, which are in general not adequate for determining the degree of survival. The number of leukocytes in 1 mm$^3$ of blood (Fig. 13) is strongly decreased after both forms of radiation. However, with a prolonged force leukopenia is, nevertheless, slightly less severe and on the day of radiation brief leukocytosis is not observed, which usually predicts a more severe course of the disease.

## Conclusion

Literature data and several views about the effect and mechanisms of the time factor on radiobiological reactions of the organism, and the nervous system in particular, have been cited in detail in our preceding works dealing with this question [1 and 7]. The present experiments verified the basic positions of earlier studies.

The severity and outcome of radiation sickness are directly dependent on dose rate. Death after an acute force is significantly higher than that after prolonged radiation. Reducing the intensity of the force by half (from 260 r/min. in past studies to 137 r/min. in this work) slightly increases survival of test guinea pigs (see Fig. 12). In this work, unlike the former, the difference in severity of leukopenia after acute and prolonged radiation was less (see Fig. 13). It is possible that this is also due to a weakening of the effect of acute radiation when its intensity is reduced from 260 to 137 r/min.

An analogous character of the action of the time factor on radiobiological effects is also found in studying the state of unconditioned motor-defense reactions.

Comparison of the changes in reflex motor activity after prolonged and
acute radiation of animals indicates significant moderation of radiation dis-
turbances in the spinal section of the central nervous system when the delivery
of radiant energy is spread out in time. If after acute radiation the increase
in the latent periods of motor reactions to all three kinds of stimulation
was recorded throughout the entire examination period (see Fig. 4), after pro-
longed radiation (see Figs. 2|and 3) inhibition of these reactions was noted
only on the 12th and 15th days of observation. The rest of the time changes in
these indices fell within the limits of those in the control group of animals
(see Fig. 1).

Statistical analysis of material, even using the low-sensitive median
test, verified the reliability of difference of changes in test indices after
acute radiation from those in control animals and those exposed to prolonged
radiation ($p < 0.01$ and $p < 0.05$). The difference in the change in these indices
between control animals and those exposed to prolonged radiation ($p < 0.05$) was
found only after analysis of the material by the more sensitive Plokhinskiy
method. We must note that changes in reflex conductivity in animals exposed
to prolonged radiation with a dose of 500 r statistically reliably did not
differ ($p \gg 0.05$) from those in animals exposed to an analogous radiation but in
a dose of 554 r (see preceding |article in this collection).

Data from this study, therefore, agree completely with the results of
earlier studies (see previous article in this collection) and verify the con-
clusion that with radiation changes in the spinal section of the central ner- |
vous system with the doses and forms of radiation we used,|the time factor has
a direct effect.

It is more complicated to evaluate the effect of the time factor on radi-
ation reactions of the vestibular analysor. A smaller change in characteristics of|
the vestibulotonic reflex with prolonged radiation cannot be indicated. The
effect of the radiant force according to the majority of test indices was two-
phase. The first phase occurred during the first 10-12 days after radiation
and the second phase later, i.e. up to the 20th day of observation. The initial
period of changes (phase I) is characterized by greater effectiveness of pro-
longed radiation. Electric activity of muscles during and after the presentation
of an adequate stimulus is reduced (with acute radiation it is slightly raised),

the latent period is strongly increased (significantly more than with acute radiation) and the length of the after-action is shortened (to the same degree as after acute radiation). This all indicates that after prolonged radiation a more severe inhibition process develops in structures of the vestibular | analysor than after an acute force.
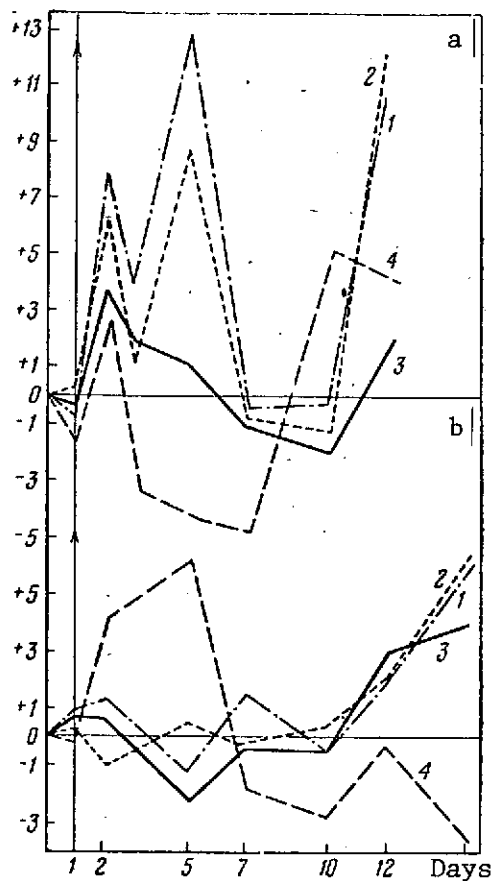
During the second phase of postradiation changes there are reverse ratios. The level of the vestibulotonic reaction and after-action is lower after acute radiation (although according to absolute values the effect of a prolonged force is equal or greater), the latent period is longer but the length of the after-action is shorter than with radiation at a low dose rate, Acute radiation, therefore, during this period causes a slightly more serious inhibiting process than radiation in large exposure. The relative increase in effectiveness of the acute force is connected, possibly, with the fact that during that time (after 10-12 days) the clinical state of the majority of animals exposed to prolonged radiation improves and a tendency is noted toward recovery of disturbed functions. The state of acutely radiated animals during this time remains quite severe, many guinea pigs die or are on the brink of death. Evidently, the severity of radiation sickness is also connected with the fact that, in the work of 1966, no pronounced phase character of postradiation changes was evident. Acute radiation then was more intense with a higher dose rate. Its damaging effect was greater, the animals died sooner and in larger number, so that the phase character of changes, evidently, simply did not appear. Lack of a direct effect of the time factor on radiobiological changes in the system of the vestibular analysor is completely verified also if we only take into account data on animals in which the state of unconditioned defense reflexes to stimulation with an electric current was studied simultaneously. In the same animals, therefore, with identical forms of exposure a different effect of the time factor is found on radiobiological reactions of different structures of the central nervous system. For the spinal section of the central nervous system acute radiation was more effective, shifts in the system of the vestibular analysor during prolonged radiation were practically unmoderated and sometimes even increased.

Slightly different ratios were noted with a change in spontaneous myoelectric activity in a state of relative rest. Increase of this parameter in the

first period after prolonged radiation indicates excitation in corresponding structures of the nervous and muscular systems. Although the changes here are quite pronounced (significantly greater than the reduction of myoelectric activity after acute radiation) the predominance of the exciting process can, evidently, nevertheless, be evaluated as the result of some moderation of the radiation force during its prolongation.

Figure 14. Individual changes in the latent period of unconditioned-defense |motor reaction and spontaneous electric activity of extensor muscles in guinea pig No. 39 (a) after acute radiation and in guinea pig No. 23 (b) after prolonged radiation.|

Symbols same as in Fig. 2.

The second phase of postradiation changes is practically the same for both forms of radiation.

In comparing changes in unconditioned reflex motor activity and vestibulo-tonic reflexes in the same animals,|it is outstanding that a change in the background bioelectric activity of muscles to a certain degree coincides with changes in the latent periods of unconditioned defense motor reactions. This is found after both acute and prolonged radiation. Depression of spinal conductivity, as a rule, is accompanied by a reduction of background bioelectric activity

of extensors (see Fig. 3, 12th, 15th, 20th day; Fig. 4, first 7 days of observation; Fig. 14, a, 3rd and 5th day; Fig. 14, b, 12th and 15th day). While a tendency toward shortening is seen in the change in latent periods of tested motor reactions, an increase in spontaneous activity of muscles is recorded (see Fig. 3, 5th day; Fig. 2, first 7 days of observation; Fig. 14, b, 5th day   /156 of observation). Such an identical direction of changes in these indices is, evidently, connected with the fact that change in spontaneous biopotentials of muscles is determined largely by the state of spinal motor centers. However, it is nevertheless impossible to indicate a strict correlation between these parameters in time. Changes in background electric activity of muscles and latent periods of defense motor reaction in the same general direction are often independent of each other. Besides the above noted synchronous changes, the following cases of correlation were noted. Increased bioelectric activity, recorded at rest, could be observed against a background of unchanged spinal conductivity (see Fig. 14, b, 2nd day; Fig. 3, 1st and 2nd day) as well as its depression (see Fig. 14, a, 2nd and 1st day of observation). At the same time depression of spontaneous electric activity could be unaccompanied by any changes in spinal conductivity (see Fig. 14, a — 7th day; Fig. 14, b — 7th and 10th day of observation). We must, however, note that increased spontaneous activity of extensors against a background of serious inhibition of spinal reactions, as well as increased spinal conductivity against a background of reduction of potentials of muscles at rest, were very insignificant, while physiologically shifts in similar directions in both indices were quite significant.

The imperfect agreement of these changes is due, evidently, to fluctuations in the level of spontaneous bioelectric activity of muscles which to some degree reflect shifts in systems not only of the motor, but also of the vestibular and tactile analysors, etc. A different kind of relation of basic nerve processes, revealed in studying spontaneous electric|activity of muscles (in comparison with parameters of strictly vestibulotonic reactions), evidently also indicates a different direction of radiation changes in functional structures of different analysor systems. Revealing the mechanisms of the different reactions to radiation and its intensity in various analysors is a very complex question and requires special research.

REFERENCES

1. Apanasenko, Z.I. In the book: "Vliyaniye faktorov kosmicheskogo poleta na funktsii tsentral'noy nervnoy sistemy" (The Effect of Space Flight Factors on Functions of the Central Nervous System). Moscow, "Nauka", 1966, p. 197.

2. Gvozdikova, Z.M. Izmeneniye spinnomozgovykh refleksov v zavisimosti ot sostoyaniya gipotalamicheskoy oblasti pri ostrom luchevom pora-zhenii u krolikov (Change in Cerebrospinal Reflexes in Relation to the State of the Hypothalamus Area During Acute Radiation Damage in Rabbits). Candidate's dissertation. Moscow, 1965.

3. Gorshkov, S.I. Skrytoye vremya|reflektornykh reaktsiy kak adekvatnyy pokazatel' funktsional'nogo sostoyaniya nervnoy sistemy (Latent Period of Reflex Reactions as an Adequate Index of the Functional State of the Nervous System). Doctoral dissertation. Moscow, 1963.

4. Zakusov, V.V. Vestnik AMN SSSR, No. 2, 1962, p. 14.                      /157

5. Kalyayeva, G.V. In the book: "Voprosy patogeneza eksperimental'noy terapii i profilaktiki luchevoy bolezni" (Questions of the Pathogenesis of Experimental Therapy and Previontion of Radiation Sickness). Moscow, Medgiz., 1960, p. 28.

6. Kuznetsova, M.A. Radiobiologiya. Vol. 1, No. 1, 1961, p. 58.

7. Kuznetsova, M.A. In the book: "Nekotorye voprosy kosmicheskoy neyro-fiziologii" (Some Questions of Space Neurophysiology). Moscow, "Nauka", 1967, p. 93.

8. Livanov, M.N. Nekotorye problemy deystviya ioniziruyushchey radiatsii na nervnuyu sistemu (Some Problems of the Effect of Ionizing Radiation on the Nervous System). Moscow, Medgiz., 1962.

9. Nuzhdin, N.I., M.D. Pomerantseva and N.N. Kuznetsova. Doklady AN SSSR, Vol. 2, No. 137, 1961, p. 438.

10. Plokhinskiy, N.A. Biometriya (Biometry). Izd-vo Mosk. gos. un-ta, 1970.

11. Remizova, I.V. In the book: "Voprosy radiobiologii i klinicheskoy radiologii" (Questions of Radiobiology and Clinical Radiology). Leningrad., 1965, p. 59.

12. Skuratovich, A.A. In the book: "Voprosy obshchey radiologii" (Questions of General Radiology). Moscow, Atomizdat., 1966, p. 294.

13. Strelin, G.S. and K.F. Galkovskaya. In the book: "Voprosy deystviya malykh doz ioniziruyushchey radiatsii na fiziologicheskiye funktsii" (Questions of the Effect of Small Doses of Ionizing Radiation on Physiological Functions). Moscow, Izd-vo AN SSSR, 1961.

14. Shapovalov, M.I. Fiziol. zhurn., Vol. 6, No. 49, 1963, p. 685.

15. Brissell, R.R. Nature, No. 4929, 1964, p. 262.

16. Lott, J.R. In: Effects of Ionizing Radiation on the Nervous System. International Atomic Energy Symposium, Vienna, 1962, p. 82.

17. Maurer, H.A. and W. Minder. Inter. J. Rad. Biol. Vol. 2, No. 2, 1960, p. 17.

18. Magnus, R. Korperstellung Monographien aus des Gesamtgebiete der Physiologie der Pflanzen und der Ture. Berlin, 1924.

19. Sato, M., G. Austin and W. Stahl. In: Response of the Nervous System to Ionizing Radiation. Academic Press, N.Y.-London, 1962, p. 561.

20. Sato, N., G. Austin and W. Stahl. In: Effect of Ionizing Radiation on the Nervous System" International Atomic Energy Symposium, Vienna, 1962, p. 93.

IV

METHODS

BIOELECTRIC INTEGRATOR

V. P. Kornil'yev

At the present time various kinds of electronic equipment are widely used for quantitative evaluation of bioelectric signals which enable the experimenter to obtain instantaneously necessary information about the bioelectric process.

For rapidly-changing processes such as myography, graphic registration using ordinary strip chart recorders is ineffective. Strip chart recorders, as a rule, can fix signals with a frequency not over 50-75 Hz, while myographic signals contain components up to 500-600 Hz or more. Oscillographic recording methods also do not make prolonged registration possible. In addition, subsequent manual analysis of graphic information is not sufficiently accurate and requires a great deal of time [1].

All the difficulties connected with graphic registration of bioelectric signals can be largely avoided by using a simple electronic instrument — an integrator [2].

This instrument, distinguished by great simplicity and reliability, is made entirely of transistors. Because of low-resistance charging-discharging circuits the instrument can be frequency tuned; with the use of electronic counters it has rather high resolution and, therefore, there are few errors connected with dead time and nonlinearity of amplitude characteristics.

Besides a discrete output signal, recorded by digit counters, the integrator also prints out results in analogous form to the strip chart recorder. A timer combined with the integrator, switching the digit counters, provides information for certain intervals of time, for example, before, during and after any action on the object. Operation of the instrument influencing the object is synchronized with that of the timer (Fig. 1).
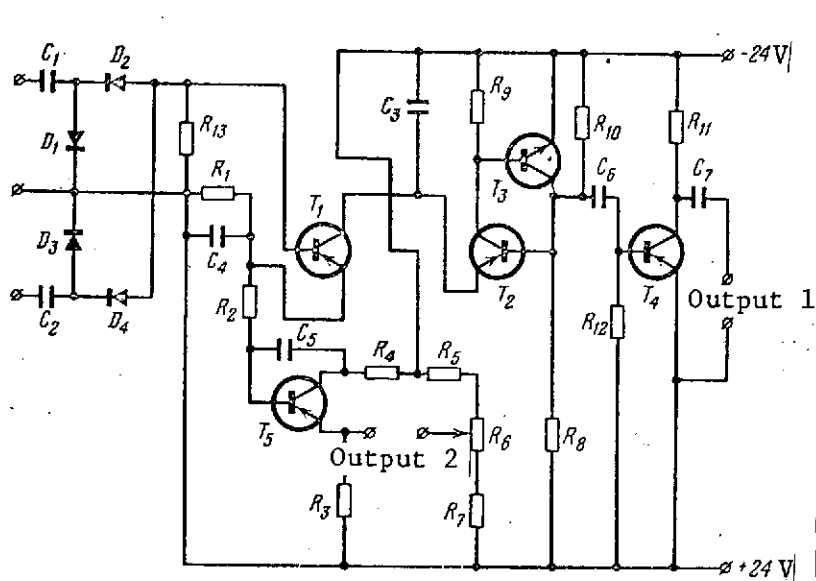
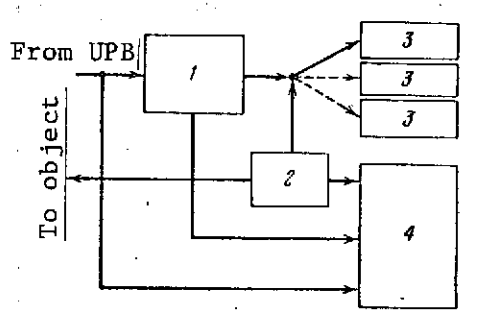Figure 1. Schematic diagram of the bioelectric integrator.



Figure 2. Block diagram of the unit.
1 — integrator of biopotentials;
2 — timer; 3 — electronic counters;
4 — strip chart recorder.

A schematic diagram of the integrator is given in Fig. 2.

The signal from the bioelectric amplifier enters a fullwave rectifier and control transistor T. The collector current of transistor $T_1$ is proportional to the instantaneous value of its signal at base. Energy storage capacitor $C_3$ is charged by the collector current of transistor $T_1$. When a certain level of voltage potential is reached at condensor $C_3$ a relay is triggered at transistors $T_2$ and $T_3$ (with different conductance), condensor $C_3$ is discharged and the relay broken. Theoretically the relay in transistors $T_2$ and $T_3$ can be replaced by a low-voltage switching diode. A negative impulse resulting from the discharge of condensor $C_3$ is amplified and reversed in phase by the amplifier to transistor $T_4$ and through the timer to the recording

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digit counter.

The mean value of the control transistor current enters the integrating $/160$
amplifier at transistor $T_5$ through integrating chain of $C_4$. From there an
analog signal, proportional to the |mean total bioelectric activity, enters the
strip chart recorder.

As a preliminary amplifier for recording the electromyographic signal we
used an amplifier with the expanded transmission band of a 4-channel encephalo-
graph (4 EEG-1). Terminal repeaters with the strip chart recorder of this
encephalograph were used for graphic recordings of electromyograms, summary
electromyograms and check points during analysis. Electronic counters were
used as digit counters.

This| instrument has been in production for a long time and has shown
good results.

## REFERENCES

1.    Kozhevnikov, V.A. and R.N. Meshcherskiy. Sovremennye metody analiza
      entsefalogrammy (Modern Methods of Encephalogram Analysis). Moscow,
      Medgiz., 1963.

2.    Gutman, S.R. In the book: "Elektronnaya apparatura dlya elektrofizio-
      logicheskikh issledovaniy" (Electronic Equipment for Electrophysio-
      logical Research). Moscow, "Nauka", 1969, p. 18.

# AUTOMATIC RHEOGRAPH

## V. P. Kornil'yev, A. T. Ugolyev

At the present time among physiologists and clinical physicians a method
of bloodless and painless circulation research — impedance rheography — is very
popular [2]. Quite varied rheographs have been described. The majority of them
are based on potentiometric or bridge methods of measuring impedance in the
test object. Both of these methods have certain inadequacies. The potentio-
metric method is extremely inaccurate, its amplitude characteristics are very
nonlinear and it has low noise stability. The advantages of this method in-
clude simplicity of design and the possibility of adjustment-free operation.

Bridge methods are very sensitive and accurate but require preliminary
balancing of active and often also reactive components of impedance. This
greatly complicates working with rheograms, especially with several channels.
It is especially complicated to take measurements when surface electrodes with
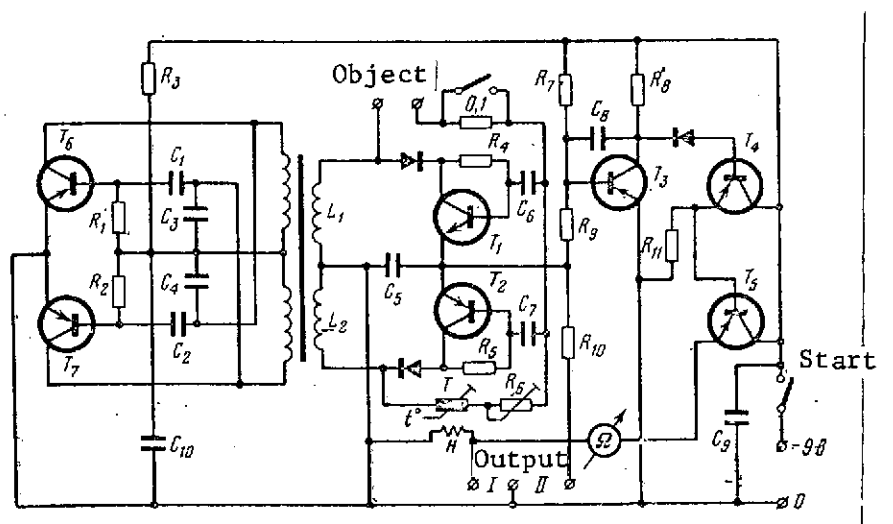
Schematic drawing of the rheograph
Symbols explained
in text

a small working area are used or when the object is moving or in a long experiment. Small changes in surface electrode resistance cause significant artifacts and require periodic fine tuning of bridge rheographs [1].

This rheograph is largely free of these shortcomings. | It combines the simplicity of operation of potentiometric rheographs and the qualities of bridge units.

An automatic fine tuning system makes it possible to avoid preliminary balancing of the bridge and completely eliminates all low-energy changes of impedance, | while pulse changes are practically undistorted. The advantages of this instrument also include the possibility of obtaining the impedance of the object directly on a point indicator dial. The instrument is especially suitable for long experiments without the interference of the experimentor.

The use of the phase method of measuring impedance largely excludes the | effect of one channel on another. The illustration presents a circuit of one channel of the instrument. The circuit |contains a 150 kc generator common to both channels, an a.c. bridge whose two arms are resistors $R_4$ and $R_5$ and resistor $R_6$, a third arm — a balancing thermoresistor and a fourth — the portion of tested tissue. Serially engaged with the object is calibrated resistance, making it possible to evaluate the amplitude of the rheographic signal.

A phase detector is engaged diagonally to the bridge in transistors $T_1$ and $T_2$ (of different |conductance). The phase detector is supplied with power by the | same coils $L_1$ and $L_2$, simplifying the design of the instrument highly. The signal of unbalance from the phase detector is amplified by a two-stage d.c. amplifier in transistors $T_3$ and $T_4$ and by a power amplifier in transistor $T_5$. A heating coil located in the thermoresistor is engaged in| the emitter chain |of transistor $T_5$. As a result negative d.c. feedback develops.

At the first moment after engagement of the instrument,|maximum current flows through the heating coil which is reduced as the bridge approaches balance. Impedance between electrodes can be estimated by the current established in the heating coil. As the thermistor–heater system has great thermal inertia, the thermistor only compensates those changes in impedance longer than 2-3 seconds. Therefore, pulse fluctuations of impedance are not reduced by the system, while lower energy fluctuations are almost completely repressed. The variable component of the signal from the d.c. amplifier enters the recording unit. An

integrating RC-filter is engaged in the chain of the emitter follower, increasing the time constant of the instrument and repressing possible relaxation fluctuations with extremely high feedback.

Resistor $R_1$ must be adjusted for initial selection of the operating range of the rheograph. The sensitivity of the d.c. instrument also depends on it. Using a MMT-1 thermoresistor with initial resistance of 2.2 kohm we were able to obtain an adjustment-free range of operation of the instrument from 60 to 1500 ohms using current in the heating coil from 15 to 90 ma; bridge unbalance with maximum current did not exceed 7.5 ohms. Temperature instability under the same conditions was about 4 ohms per 1°, which corresponded approximately to the 0.25 reading on the impedance indicator.

Because of the extent of balance autoregulation of the bridge the instrument made it possible for experiments to be conducted by the most varied methods. For example, rheographic studies of high-frequency fluctuations in | vascular blood flow were possible with the use of microelectrodes 10-20 μ in diameter. At the place where the microelectrode comes in contact with the wall of the exposed vessel, there must be low-energy displacements and the use of ordinary rheographs becomes extremely difficult. The autobalancing method, with the use of specially shaped electrodes, made it possible to study the dependence of electric conductivity on the linear rate of blood flow and pressure on vascular walls. To record second-order waves and lower-energy waves, we used a direct signal from the heating coil of the thermistor.          /163

This instrument can also be used for many other measurements when maximum interest is being given to a rapidly changing signal from ohmic transmitters, for example, rapid changes in temperature (if a thermoresistor is used as the transmitter), pressure, etc.

## REFERENCES

1.    Arnautov, A.L.  In the book: "Sovremennye pribory i tekhnika fiziologicheskogo eksperimenta" (Modern Instruments and the Technique of Physiological Experimentation). Moscow, "Nauka." 1969, p. 59.

2.    Hill, R.V.  J. Appl. Physiol. Vol. 22, No. 1, 1967, p. 161.

# CARDIAC RHYTHM DYNAMICS ANALYZER

V. N. Kornil'yev,  E. A. Bogdanova

As is known, significant changes in cardiac rhythm reflect disturbances in circulation which are a serious danger in various medico-biological experiments.

In addition, the frequency of cardiac rhythm is a delicate index of the body's reaction in response to space flight factors (for example, emotional stress, gravitational overloads, weightless conditions), as well as functional loads during training.

In conducting initial experiments on animals, it was noted particularly that in a state of weightlessness sinus arrhythmia increases sharply. Later studies established that so-called "space arteria" is connected with increased tone of the vagus nerve but stress reactions, on the other hand, are accompanied by increased stability of cardiac rhythm with greater activity of the sympathetic nervous system. Later in-depth study of cardiac rhythm revealed "cardiac" and "extracardiac" types of compensation [3].

The frequency of heart contractions is a simple, readily available parameter recorded with uncomplicated transmitters and easily telemetered during a space experiment. However, analysis of prolonged EKG recordings presents well-known difficulties and direct mechanical analysis is quite complex, requiring expensive equipment, and is not always possible in everyday experiments.

We have suggested a rather simple instrument to analyze the R-R series of /164 intervals by the length of each interval and average frequency of heart contractions with a time constant on the order of 20 seconds. In addition, this instrument can determine the number of heart contractions per unit of time with a mechanical counter (which also serves as a sonic indicator of pulse) and judge the rhythm frequency by a pointer instrument. An automatic control system gives sound signals when changes in the frequency of rhythm exceed permissible limits. A system for compensating the invariable part of cardiac rhythm makes it possible to record all changes in rhythm with great sensitivity.

Figure 1. Block diagram of an analyzer
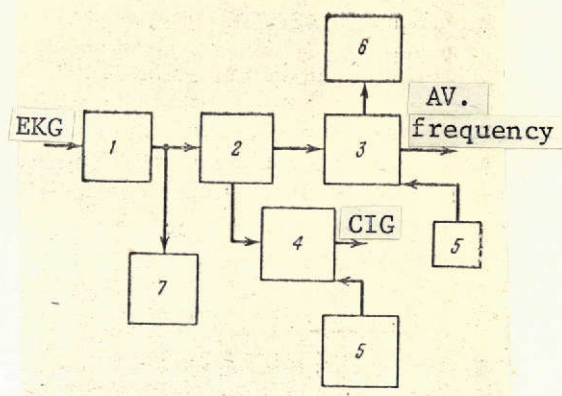of the dynamics of cardiac rhythm structure.
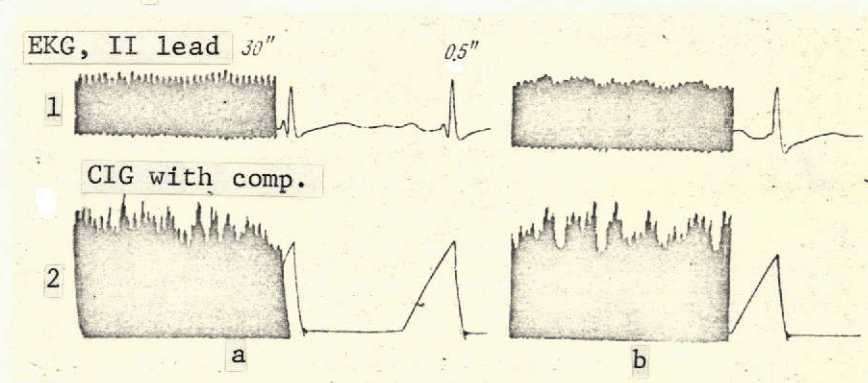
Symbols explained in text.



Figure 2. Change in the structure of
cardiac rhythm under the influence of
small doses of neuroleptic analgesics.

a — before introduction of the drugs;
b — after introduction; 1 — EKG; 2 —
CIG with compensation.



A block diagram of the instrument is given in Fig. 1. The instrument con-
sists of the following functional units: amplitude discriminator (1) to dis-
tinguish R notches from the cardiogram and normalize their amplitude. A
driven multivibrator (2) forms square pulses of standard amplitude and length
to each R notch. After passing through the integrating block (3) these pulses
are a signal of average pulse rate. The cardiointervalographic unit contains
a generator of sawtooth pulses (4) whose amplitude is proportional to the time /165
between RR notches, which are also a signal of the cardiointervalogram (CIG).
A compensation system (5) supplies compensating voltage simultaneously to a
medium-frequency producing unit and the cardiointervalogram unit. By compen-
sating the invariable part of these signals, the other part can be recorded
with great sensitivity. The medium-frequency signal of impulses is compared
with standard voltage; the latter is established in calibrating the instrument.
When the medium-frequency signal exceeds (or falls below) standard the signal
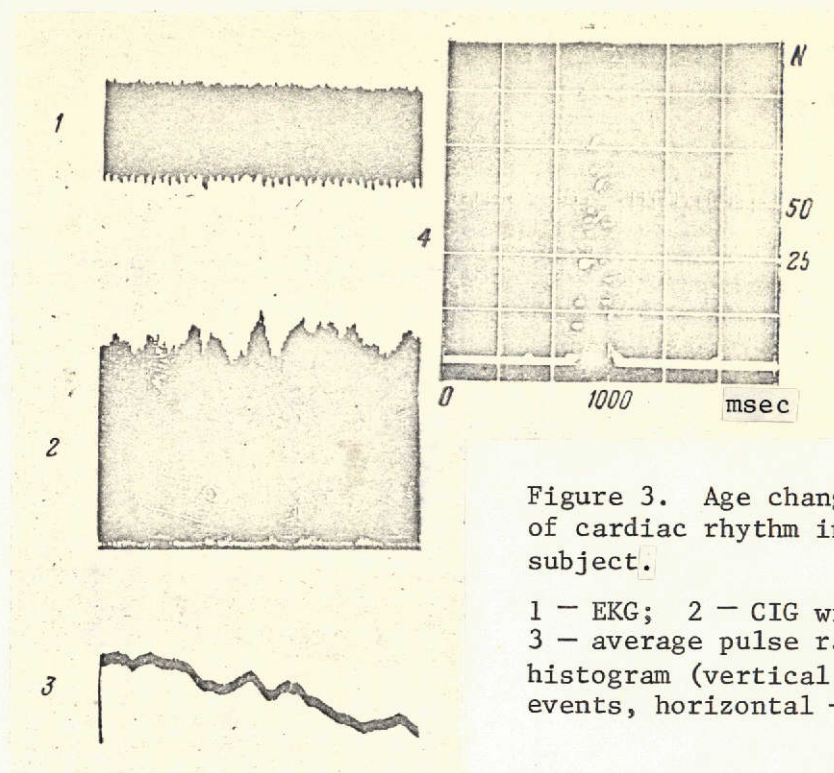unit (6) is engaged.

Figure 3. Age changes in the structure of cardiac rhythm in a 49-year-old subject.

1 — EKG;  2 — CIG with compensation; 3 — average pulse rate;  4 — integral histogram (vertical axis — number of events, horizontal — time axis).

In addition, impulses from the amplitude discriminator (1) enter the mechanical recorder unit (7) consisting of a driven multivibrator and a mechanical counter controlled by the multivibrator.  Some recordings made using this instrument to study healthy and sick persons in the departmental surgery clinic of MMI I imeni Sechenov are given below.

Fig. 2 gives several curves reflecting change in the structure of cardiac rhythm under the influence of small doses of neuroleptic analgesics. On the upper edge of the silhouette of the cardiointervalogram (CIG) (in Fig. 2, a) periodic fluctuations are seen in both respiratory and nonrespiratory slow waves of cardiac rhythm (2, 5).  Under the influence of the drugs the picture of slow waves changed (Fig. 2, b).

Age changes in cardiac rhythm were specially studied in works [1, 4]. Fig. 3, 1, gives curves of a 49-year-old patient with symptoms of atherosclerosis.  The CIG readily shows slow waves of various periods and amplitudes.  In comparison with the CIG in Fig. 2, a, the lack of respiratory fluctuations of cardiac rhythm is noticeable.
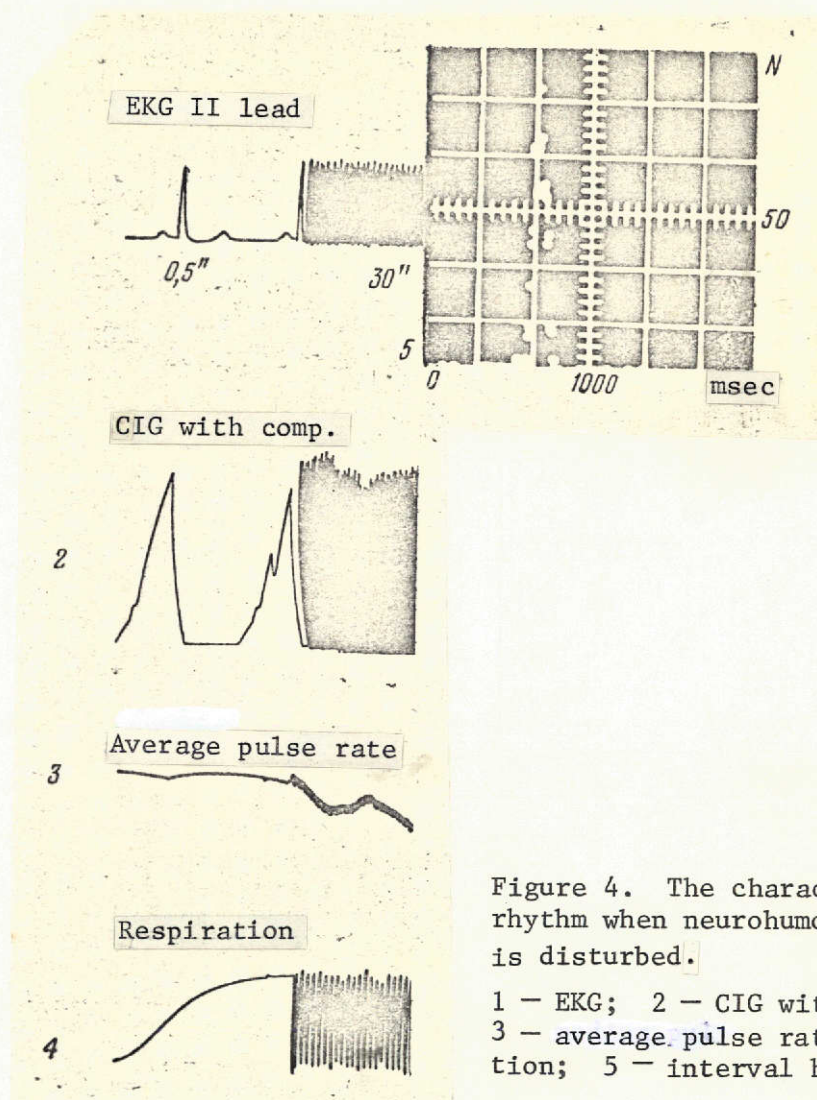
Figure 4. The character of cardiac rhythm when neurohumoral regulation is disturbed.

1 — EKG;  2 — CIG with compensation; 3 — average pulse rate;  4 — respiration;  5 — interval histogram.

The variance of the length of RR intervals is easy to see in statistical
analysis.  Fig. 3, 5, gives RR intervals — histograms obtained with a specialized electronic machine.  Comparison of these histograms with the CIG shows that changes in the frequency of cardiac rhythm in this case are connected with nonrespiratory slow waves.

There are important changes in the structure of cardiac rhythm with various disturbances of neurohumoral regulation.  In this sense, studies of changes in functions of the thyroid gland are extremely indicative.  Fig. 4

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gives curves for a patient with thyrotoxicosis, typical of high frequency and stability of cardiac rhythm. The CIG shows respiratory waves; however, their character is different from those in Fig. 2, a. The interval does not increase evenly but stepwise, change in frequency of rhythm was discrete due to the unique shape of the CIG (Fig. 4, 2).

These examples show that curves obtained with the help of a "cardiac rhythm dynamics analyzer" are extremely sensitive to change in the state of the myocardium and central mechanisms responsible for regulation of cardiac rhythm. Evidently, the value of data obtained using this instrument will increase with the development of our knowledge of the structure and function of important sections of the heart.

We must note that this principle of analyzing medical information can also be applied to other biological signals such as EEG, EMG, etc. Because of its simplicity and universality, this instrument can find wide application in preparing and conducting various medico-biological experiments.

## REFERENCES

1.  Bayevskiy, R.M., Yu.N. Volkov and P.G. Nidekker. Matematicheskiye metody analiza serdechnogo ritma (Mathematical Methods of Analyzing Cardiac Rhythm). Moscow, "Nauka", 1968.

2.  Zatsiorskiy, V.N. and S.K. Sarsaniya. In the book: "Matematicheskiye metody analiza serdechnogo ritma" (Mathematical Methods of Analyzing Cardiac Rhythm). Moscow, "Nauka", 1968, p. 31.

3.  Parin, V.V., R.M. Bayevskiy, Yu.N. Volkov and O.G. Gazenko. Kosmicheskaya kardiologiya (Space Cardiology). Leningrad, "Meditsina", 1967, p. 195.

4.  Yanushkevichus, E., D. Zhemaytite, I. Yushkenas and G. Pargyauskas. Statisticheskaya elektrofiziologiya, chast' 1. Materialy simpoziuma 12-18 avgusta (Statistical Electrophysiology, Part 1. Material of Symposium, August 12-18). Palanga-Vilnius, 1968, p. 674.

5.  Fleisch, A. and R. Beckman. Ztschr. Ges. exp. Med. No. 80, 1932, p. 487.

ABSTRACTS

UDK 612.833.81;613.693

New Data on the Combined Effect of Space Flight Factors on the Central Nervous /170/
System. Livshits, N.N. In the collection: "Funktsii tsentral'noy nervnoy
sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radi-
atsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System under
the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and
Vibration)]. 1973. p. 1.

The article generalizes results of studies published in this collection
and compares them with earlier published studies by this group of authors and
literature data.

The role of changes in nonspecific resistance and the specific effects of
vibration and accelerations in a combined force of dynamic factors and ionizing
radiations is discussed. It is shown that existing data still give no basis
for connecting observed phenomena with phase changes in nonspecific resistance,
although, according to literature data, such a connection is very probable.
At the same time the influence of vibration on radiation effects soon after the
force of this dynamic factor can be well explained by phase changes in oxidizing
metabolism, specific for vibration.

Results of studies of the effect of vibration, radiation and a combination
of these agents on conditioned reflexes and maze learning are discussed.

Data showed that there are forms of higher nervous activity with varying
degrees of reliability and are, therefore, differently damaged under the effect |
of stress factors. An explanation of highly reliable mechanisms of several
behavioral reactions is suggested.

48 references.

UDK 612.886:613.693

Study of Remote After-action of Accelerations on Reactions of the Vestibular
Analysor to Radiation. Apanasenko, Z.I. In the collection: "Funktsii tsentral'-
noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziru-
yushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous
System under the Combined Effect of Stress Factors (Ionizing Radiation, Acceler-
ations and Vibration)]. 1973. p. 16.

Guinea pigs were used to study changes in radiation reactions of the vestibular analysor (total 500 r, 169 r/min.) under the influence of centrifuging (+8g$_x$, 15 min.), 7 days before radiation. A complex interrelation is found between forces used and predominance of the protective effect of the dynamic factor on subsequent radiation reactions. Radiation damage to the function of the vestibular analysor (according to characteristics of the vestibulotonic reflex) were subject to the moderating effect of preliminary centrifuging in much larger degree than the clinical state or survival of the animals. The effectiveness of the modifying effect of the dynamic factor with a weak interval between forces was not less (and sometimes somewhat greater) than that with an interval of three days.
10 illus. 27 ref.


UDK 612.886:613.693

The Effect of Brief Preliminary Centrifuging and Acute Gamma Radiation on the State of the Vestibulotonic Reflex with a Weak Interval Between Forces. Apanasenko, Z.I. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p. 34.

Guinea pigs were used to study changes in radiation reactions of the vestibular analysor (total 500 r, 136 r/min.) under the influence of brief centrifuging (−10g$_x$, 4 min.) 7 days before radiation. It is shown that the the character of brief tenfold overload (in a chest-back direction) on subsequent radiation reactions did not basically differ from earlier established /171 regularities in the interaction of radiation and 15-minute 8-fold overload in this direction and with the same interval between forces. There is a protective effect of preliminary centrifuging; this effect is clearly expressed by characteristics of the vestibulotonic reflex and to a much lesser degree by survival and the clinical state of the animals.
8 illus.

Comparison of the Isolated and Combined Action of Vibration and Ionizing Radiations on Conditioned Reflexes and Maze Learning of Rats. Livshits, N.N., Meyzerov, Ye.S., Zakirova, R.M., Tikhaya V. A. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p. 43.

The purpose of the work was to compare resistance to stress factors (vibration, radiation and a combination of these agents) of various kinds of higher nervous activity. To this end the effect of these factors on conditioned reflex activity of rats was studied under methodological conditions as similar as possible to those in which earlier Ye. M. Skobeyev studied the effects of these forces on the development and maintenance of maze learning.

It is shown that a three-fold force of vertical vibration (70 cps, amplitude of 0.4 mm, 15 min.),general x-ray radiations (single doses of 50 r) and a combination of these forces caused a reliable lengthening of the latent period of the conditioned reflex.

In rats exposed to radiation inhibition of differentiation (according to the index of the latent period) was also observed. Analogous forces in the tests of Ye. M. Skobeyev caused no reliable deterioration of maze learning. This indicates that some forms of higher nervous activity are more damaged by unfavorable forces and are more reliable.
4 illus. 16 ref.

Study of the Effect of Vibration, Radiations and a Combination of These Factors on Conditioned Reflexes and Maze Learning in Tests on the Same Animals. Livshits, N.N., Meyzerov, Ye.S., Zakirova, R.M., Tikhaya, V.A. In the collection: Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System under the Combined Effect of Stress

Factors (Ionizing Radiation, Accelerations and Vibration )]. 1973. p. 55.

The purpose of the work was further study of the comparative resistance to stress factors (vibration, radiation and their combination) of various kinds of higher nervous activity and to test the possibility of summation of effects of radiation and dynamic factors.

This phenomenon was recorded in a preceding work, but could not be reproduced afterward. To this end, in tests on the same animals, the effect of three vibrations (70 cps, 0.4 mm, 15 min.), general x-ray radiations in single doses of 50 r and a combination of these factors on conditioned reflexes and maze learning was studied.

The earlier stated assumption that there are forms of higher nervous activity more damaged by stress factors (conditioned reflexes) and more reliable (maze learning) was verified and an explanation offered of the mechanisms of this phenomenon.

The possibility of summation of the effects of vibration and ionizing radiations is shown and the relative difficult reproduction of this effect noted. 7 illus. 2 tables, 9 ref.

UDK 612.573:613.693

Change in Oxidizing Metabolism of Nerve Tissue in Connection with the Radio-    /172
protective Effect of General Vertical Vibration. Luk'yanova, L.D., Murashko,
L.M.    In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kom-
binirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i
vibratsii)" [Functions of the Central Nervous System Under the Combined Effect
of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p.68.

Initial changes in oxidizing metabolism of the central nervous system, re-
sulting from vibration stimulation, also affect and significantly determine the
development and course of radiation sickness. With radiation against a back-
ground of postvibration activity of oxidizing metabolism of brain tissue, the
development of radiation sickness and attendant symptoms is aggravated. Simul-
taneously observed are phase changes in the work of the respiratory chain. Ra-
diation during the period of inhibition of processes connected with the utili-

zation of oxygen have some alleviating effect on the course of development of radiation sickness and cause less severe energy disturbances.

5 illus. 1 table, 7 ref.

Basic Regularities in the Combined Effect of Dynamic Factors and Radiations on the Functions of the Central Nervous System. Livshits, N.N., Apanasenko, Z.I., Klimovitskiy, V.Ya., Kuznetsova, M.A., Luk'yanova, L.D., Meyzerov, Ye.S. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration )]. 1973. p. 80.

The combined effect of general vertical vibration (70 cps, 0.4 mm, 14 min.), lateral accelerations (8-10 g, 4-15 min.) and general x-ray and gamma radiations in doses of 50-500 r on several functions of the central nervous system were studied. Radiations were produced from 3 minutes to 20 days after the dynamic factor.

A connection was established between the type of reaction and the strength of the effect of the dynamic factor in separate application.

The dynamic factor had a more significant influence on the effect of a combined force according to these indices than radiation in lethal doses.

The radioprotective effect of vibration on somatic indices in our tests appeared only under conditions of postvibration inhibition of oxidizing processes. For the development of a certain type of reaction of the central nervous system, the functional state of the latter during radiation was of no decisive importance. A combination of three possible mechanisms of the effect of dynamic factors on radiation reactions of the central nervous system was suggested.

1. Interaction of basic nerve processes developing under the influence of the applied factors. It can conform to the principle of the dominant.

2. Specific effect of dynamic factors on tissue metabolism.

3. Neuroendocrine effects providing a long after-action of dynamic factors.

The initial mechanism of the effect of accelerations is considered to be hypoxic stress and next, changes in the function of the hypophysis-adrenal

system and energy metabolism. These changes have the character of a damping vibrational process; its phase is responsible for the radiosensitivity of the organism.

5 tables, 36 ref.

UDK 612.13:613.693

Some Characteristics of Hydrostatic Pressure Distribution in the Vascular System During Rotary Accelerations. Klimovitskiy, Z.I., Pastorye, G.L. In /173 the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p. 109.

The article discusses differences between pressure distributions with rotary and straight uniformly-accelerated pressure. The position of a hydrostatically indifferent point was studied and the value of this parameter for evaluating hemodynamic disturbances was noted. Conditions were determined for a break in the hydrostatic column with rotation around an axis passing through the body. The role of dynamic and static pressure elements in the formation of total pressure distribution in the vascular system is discussed. An example is given of correction for the dynamic component in plotting a distribution curve according to experimental data.
2 illus. 22 ref.

UDK 612.573:613.693

Comparative Study of Oxidizing Metabolism of Nerve Tissue with Vibration Stimulation in vivo and in vitro. Luk'yanova, L.D., Murashko, L.M. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Radiation)]. 1973. p. 124.

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A study was conducted of the state of the respiratory chain of nerve tissue in animals exposed to the effect of vibration. Increase in the respiratory activity of brain slices after 5-minute vibration of the animals and its reduction after 15 minutes was shown, verifying the metabolic nature of changes recorded with an "oxygen cathode" in vivo. These changes are accompanied by change in the work of the respiratory chain, they are increased with multiple vibration of |the animals and reproduced with vibration of brain slices.

6 illus. 17 ref.

UDK 612.833:81:613.693

The Effect of Vibration on the Development and Maintenance of Maze Learning in Rats. Skobeyev, Ye.M. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov| (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Radiation)]. 1973. p. 138.

The effect of general vertical vibration with a frequency of 70 cps, amplitude of 0.4 mm, lasting 15 min. produced three times at two-week and one-week intervals, caused in rats a mild and statistically unreliable increase in | the latent period of a maze run. No reduction in the rate of crossing the maze was observed. The average number of errors in crossing the maze in test rats was reliably lower than in the controls.

This is considered to be a reaction of moderate stress, accompanied by hypercompensation. |

3 illus. 22 ref.

UDK 612.833:613.693

Dependence of the Effect of General Gamma Radiations on Cerebrospinal Reflexes of Guinea Pigs on Dose Rate. Kuznetsova, M.A. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov

(ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central
Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation,
Accelerations and Vibration)].  1973.  p. 147.

Change in the functional state of the cerebrospinal reflex arc during
acute (dose rate 137 r/min) and prolonged (dose rate 0.6 r/min.) general
radiation in doses of 554 r was studied in guinea pigs.  This state was
evaluated by the change in thresholds of excitability and the latent period
of the unconditioned reflex defense general motor reaction in response to
electric skin stimulation of the hind paw.  Results indicate the moderating
effect of a prolonged dose and verify an earlier conclusion (Kuznetsova, 1967)
that with the forms and doses of radiation used there is a direct effect of
the time factor on test indices.
10 illus. 13 ref.


UDK 612.833.886:613.693

On the Role of the Time Factor in Radiation Reactions of the Vestibular
Analysor and Spinal Section of the Central Nervous System.  Apanasenko Z. I.,
Kuznetsova M. A.  In the collection: "Funktsii tsentral'noy nervnoy sistemy pri
kombinirovannom deystvii stress-faktorov| (ioniziruyushchey radiatsii, uskoreniy
i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect
of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p.161.

On the same animals (guinea pigs) change in vestibulotonic and cerebro-
spinal unconditioned reflex reactions was studied after acute (dose rates
137 r/min. and 260 r/min.) and prolonged (dose rate 0.6 r/min.) gamma radiation
in doses of 500 r.  Results indicate a different effect of the time factor on
radiobiological reactions of different structures of the central nervous system.
For the spinal section of the central nervous system acute radiation was more
effective, shifts in the system of the vestibular analysor were practically un-
moderated with prolonged radiation and sometimes even increased.
14 illus. 20 ref.

UDK 621.3.038

Bioelectric Integrator. Kornil'yev, V.P. In the collection: "Funktsii tsentralnoy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p. 180.

A simple transistor integrator of biological signals with high linearity and good resolution is described. This instrument can convert an input signal to digital and analog form.
2 illus. 2 ref.


UDK 621.3.038.

Automatic Rheograph. Kornil'yev, V.P., Ugolyev, A.T. In the collection: "Funktsii tsentral'noy nervnoy sistemu pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p. 183.

Described is a bridge rheograph with automatic balance to take measurements during prolonged experiments and in the presence of electrode interference. Balance in the bridge of the rheograph is maintained by feedback through a thermistor heated with current from the output signal.

The instrument has been used in various physiological experiments, for example, to study rapid fluctuations in blood flow.
1 illus. 2 ref.


UDK 621.3.038

Cardiac Rhythm Dynamics Analyzer. Kornil'yev, V.P., Bogdanova, E.A. In the collection: "Funktsii tsentral'noy nervnoy sistemy pri kombinirovannom deystvii stress-faktorov (ioniziruyushchey radiatsii, uskoreniy i vibratsii)" [Functions of the Central Nervous System Under the Combined Effect of Stress

Factors (Ionizing Radiation, Accelerations and Vibration)]. 1973. p. 186.

An instrument is suggested for rapid analysis of the dynamics of cardiac rhythm. The instrument analyzes the length of a number of intervals and average frequency of heart contractions per unit of time with a counter. A system of compensating the invariable part of cardiac rhythm makes it possible to record all parameters with great sensitivity.

Parameters are given for using the instrument in several medico-biological studies.

4 illus. 5 ref.